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WO 01/54507 A1

(54) Title: METHODS FOR KILLING NEMATODES AND NEMATODE EGGS USING OXADIAZOLE AND OXAIMIDAZOLE COMPOUNDS

(57) Abstract: Methods and compositions for the control of nematodes are disclosed. Specifically, the subject substituted oxadiazole anthelmintic compounds have been found to advantageously control nematodes at concentrations which are non-phytotoxic. The anthelmintic compounds can be used in conjunction with other nematicidal agents such as free fatty acids, fatty acid salts, avermectins, ivermecin, and milbemycin. In another embodiment, the subject invention further provides methods for killing the eggs of nematodes. Thus, the subject invention further relates to the surprising discovery that certain compounds have ovicidal activity against nematode eggs.

DESCRIPTION

METHODS FOR KILLING NEMATODES AND NEMATODE EGGS USING OXADIAZOLE AND OXAIMIDAZOLE COMPOUNDS

Cross-Reference to a Related Application

This application claims the benefit of U.S. Provisional Application No. 60/179,005, filed January 28, 2000.

Background of the Invention

Nematodes are important plant pests which cause millions of dollars of damage each year to turf grasses, ornamental plants, and food crops. Efforts to eliminate or minimize damage caused by nematodes in agricultural settings have typically involved the use of soil fumigation with materials such as chloropicrin, methyl bromide, and dazomet, which volatilize to spread the active ingredient throughout the soil. Such fumigation materials can be highly toxic and may create an environmental hazard. Various non-fumigant chemicals have also been used, but these, too, create serious environmental problems and can be highly toxic to humans.

The accepted methodology for control of nematodes afflicting animals has centered around the use of the drug benzimidazole and its congeners. The use of these drugs on a wide scale has led to many instances of resistance among nematode populations (Prichard, R.K. *et al.* [1980] "The problem of anthelmintic resistance in nematodes," *Austr. Vet. J.* 56:239-251; Coles, G.C. [1986] "Anthelmintic resistance in sheep," In *Veterinary Clinics of North America: Food Animal Practice*, Vol 2:423-432 [Herd, R.P., Eds.] W.B. Saunders, New York).

The pesticidal activity of avermectins is well known. The avermectins are disaccharide derivatives of pentacyclic, 16-membered lactones. They can be divided into four major compounds: A_{1a}, A_{2a}, B_{1a}, and B_{2a}; and four minor compounds: A_{1b}, A_{2b}, B_{1b}, and B_{2b}.

The organism which produces avermectins was isolated and identified as *Streptomyces avermitilis* MA-4680 (NRRL-8165). Characteristics of the avermectin producing culture and the fermentation process are well documented and known to those

skilled in the art (Burg, R.W. *et al.* [1979] "Avermectins, New Family of Potent Anthelmintic Agents: Producing Organism and Fermentation," *Antimicrob. Agents Chemother.* 15(3):361-367). The isolation and purification of these compounds is also described in U.S. Patent No. 4,310,519, issued January 12, 1982.

Another family of pesticides produced by fermentation are the milbemycins, which are closely related to the avermectins. The milbemycins can be produced by a variety of *Streptomyces* and originally differed from the avermectins only in the C-13 position. The milbemycins and their many derivatives are also well known to those skilled in the art and are the subject of U.S. patents. See, for example, U.S. Patent No. 4,547,520.

While the avermectins were initially investigated for their anthelmintic activities, they were later found to have other insecticidal properties, although the degree varies. The activity of avermectins must generally be determined empirically.

22,23-dihydroavermectin B_1 is a synthetic derivative of the avermectins and has been assigned the nonproprietary name of ivermectin. It is a mixture of 80% 22,23-dihydroavermectin B_{1a} and 20% 22,23-dihydroavermectin B_{1b}. Ivermectin has been tested on a variety of laboratory and domestic animals for control of nematodes, ticks, and heartworms.

Avermectin B_{2a} is active against the root-knot nematode, *Meloidogyne incognita*. It is reported to be 10-30 times as potent as commercial contact nematicides when incorporated into soil at 0.16-0.25 kg/ha (Boyce Thompson Institute for Plant Research 58th Annual Report [1981]; Putter, I. *et al.* [1981] "Avermectins: Novel Insecticides, Acaracides, and Nematicides from a Soil Microorganism," *Experientia* 37:963-964). Avermectin B_{2a} is not toxic to tomatoes or cucumbers at rates of up to 10 kg/ha. Avermectin B_1 is a combination of avermectin B_{1a} (major component) and avermectin B_{1b}. It has demonstrated a broad spectrum of insecticidal activities. The data indicate that avermectin B_1 is primarily a miticide, although it is also effective on the Colorado potato beetle, potato tuberworm, beet armyworm, diamondback moth, gypsy moth, and the European corn borer.

The use of avermectins in various agricultural applications has been described in publications and patents. The use of avermectin with spray oils (lightweight oil compositions) has been described. See, for example, U.S. Patent No. 4,560,677 issued

December 24, 1985; EPO applications 0 094 779 and 0 125 155; and Anderson, T.E., J.R. Babu, R.A. Dybas, H. Mehta (1986) *J. Econ. Entomol.* 79:197-201.

There is a continuing need for new, alternative materials and methods useful for killing nematodes.

Brief Summary of the Invention

The subject invention concerns substituted compositions and processes for controlling nematodes. In one embodiment, the subject invention comprises the use of substituted oxadiazoles to control nematodes which infest and afflict animals. Nematodes which infest plants or the situs of plants can also be controlled using the methods and compositions of the subject invention, as can other acarid and arthropod pests.

Preferred compounds useful according to the subject invention include substituted oxadiazole compounds, and can be represented by the Formulae I, II, III, IV, and V as further described herein.

1. A urea derivative of the following Formula I:

$$Ar\text{-}(Alk)_{0\text{-}1}\text{-}NH\text{-}CO\text{-}NR^1\text{-}Alk\text{-}R^2 \qquad \text{(Formula I)}$$

wherein Ar is aryl or heteroaryl optionally substituted by one or more R^3 groups;

each Alk is a linear or cyclic alkylene radical of up to 8 C atoms;

R^1 is H or $C_{1\text{-}6}$ alkyl;

R^2 is heteroaryl or heterocycloalkyl optionally substituted by Ar, or forms such a group by cyclisation with R^1; and

R^3 is OH, halogen, CF_3, OCF, or a group selected from NH_2, $SO_2\text{-}C_{1\text{-}6}$ alkyl, $C_{6\text{-}10}$ aryl,

$C_{6\text{-}10}$ aryloaxy, $C_{5\text{-}6}$ cycloalkyl, $C_{1\text{-}5}$ alkoxy, and $C_{1\text{-}6}$ alkyl, said group being optionally substituted by OH, $C_{1\text{-}6}$ alkoxy, $C_{1\text{-}6}$ alkyl, phenyl, halogen, or CF_3.

Particularly preferred anthelmintic compounds according to Formula I are exemplified herein by compounds represented by structures 1-10 (depicted in Figures 1-10, respectively), which have been assigned the respective reference numbers:

AKC 111 (STRUCTURE 1),

AKC 112 (STRUCTURE 2),

AKC 113 (STRUCTURE 3),

AKC 107 (STRUCTURE 4),

AKC 114 (STRUCTURE 5),
AKC 108 (STRUCTURE 6),
AKC 115 (STRUCTURE 7),
AKC 116 (STRUCTURE 8),
AKC 117 (STRUCTURE 9), and
AKC 118 (STRUCTURE 10).

2. A heterocycle-substituted amide of the following Formula II:

$$Ar\text{-}(Alk)_{0\text{-}1}\text{-}NH\text{-}CO\text{-}Het \qquad \text{(Formula II)}$$

wherein Ar is aryl or heteroaryl optionally substituted by one or more R^3 groups;

each Alk is an optionally cyclic alkylene radical of up to 8 C atoms;

Het is heteroaryl or heterocycloalkyl optionally substituted by Ar and/or R^3; and

R^3 is OH, halogen, CF_3, OCF_3, or a group selected from NH_2, SO_2alkyl, $C_{6\text{-}10}$aryl, $C_{1\text{-}6}$ alkoxy, and $C_{1\text{-}6}$ alkyl, said group being optionally substituted by OH, $C_{1\text{-}6}$ alkoxy, $C_{1\text{-}6}$ alkyl, phenyl, halogen, or CF_3.

Particularly preferred anthelmintic compounds according to Formula II are exemplified herein by compounds represented by Structures 11-25 (depicted in Figures 11-25 respectively), which have been assigned the respective reference numbers:

AKC 119 (STRUCTURE 11),
AKC 110 (STRUCTURE 12),
AKC 120 (STRUCTURE 13),
AKC 121 (STRUCTURE 14),
AKC 2153 (STRUCTURE 15),
AKC 122 (STRUCTURE 16),
AKC 104 (STRUCTURE 17),
AKC 123 (STRUCTURE 18),
AKC 124 (STRUCTURE 19),
AKC 125 (STRUCTURE 20),
AKC 105 (STRUCTURE 21),
AKC 126 (STRUCTURE 22),
AKC 102 (STRUCTURE 23),
AKC 103 (STRUCTURE 24), and

AKC 171 (STRUCTURE 25).

3. A secondary arylamine of the following Formula III:

Ar-NH-CHR-CH_2-CO-Y (Formula III)

wherein Ar is aryl or heteroaryl optionally substituted by one or more R^3 groups;

R is aryl, heteroaryl, or heterocycloalkyl optionally substituted by R^3 ;

Y is C_{1-6} alkyl, aryl, or heteroaryl optionally substituted by R^3 ;

or R and Y together form a cycloalkyl or heterocycloalkyl ring; and

R^3 is OH, halogen, CF_3, OCF_3, or a group selected from NH_2, SO_2 alkyl, C_{6-10} aryl, C_{1-6} alkoxy, and C_{1-6} alkyl, said group being optionally substituted by OH, C_{1-6} alkoxy, C_{1-6} alkyl, phenyl, halogen, or CF_3.

Particularly preferred anthelmintic compounds according to Formula III are exemplified herein by compounds represented by Structures 26-31 (depicted in Figures 26-31, respectively), which have been assigned the respective reference numbers:

AKC 128 (STRUCTURE 26),

AKC 129 (STRUCTURE 27),

AKC 130 (STRUCTURE 28),

AKC 131 (STRUCTURE 29),

AKC 132 (STRUCTURE 30), and

AKC 133 (STRUCTURE 31).

4. A diaryl amine of the following Formula IV:

Ar-$(Z)_{0-1}$-Ar-$(CH_2)_{0-1}$-NHR (Formula IV)

wherein Ar is aryl or heteroaryl optionally substituted by one or more R^3 groups;

Z is NH, O, S, or Alk; and Alk is a linear or cyclic alkylene radical of up to 8 C atoms

wherein said radical optionally includes one or more heteroatoms;

R is H or R^3,

R^3 is OH, halogen, CF_3, OCF_3, or a group selected from NH_2, SO_2 alkyl, C_{6-10} aryl, C_{1-6} alkoxy, and C_{1-6} alkyl, said group being optionally substituted by OH, C_{1-6} alkoxy, C_{1-6} alkyl, phenyl, halogen, or CF_3.

Particularly preferred anthelmintic compounds according to Formula IV are exemplified by compounds represented by structures 32-37 (depicted in Figures 32-37, respectively), which have been assigned the respective reference numbers:

AKC 109 (STRUCTURE 32),
AKC 134 (STRUCTURE 33),
AKC 135 (STRUCTURE 34),
AKC 136 (STRUCTURE 35),
AKC 137 (STRUCTURE 36), and
AKC 138 (STRUCTURE 37).

5. A substituted heteropolycyclic compound of the following Formula V:

Het_2-Q (Formula V)

wherein Het_2 is two or three fused aromatic rings including one or more heteroatoms selected from N, O and S, and Q includes at least one substituent selected from OH, $COOR^3$ and $CONHR^3$, and optionally also another substituent selected from alkyl and alkenyl of up to 10 C atoms;

wherein R^3 is OH, halogen, CF_3, OCF_3, or a group selected from NH_2, SO_2 alkyl, C_{6-10} aryl, C_{1-6} alkoxy, and C_{1-6} alkyl, said group being optionally substituted by OH, C_{1-6} alkoxy, C_{1-6} alkyl, phenyl, halogen, or CF_3.

Particularly preferred anthelmintic compounds according to Formula V are exemplified by compounds represented by structures 38-43 (depicted in Figures 38-43, respectively), which have been assigned the respective reference numbers:

AKC 139 (STRUCTURE 38),
AKC 140 (STRUCTURE 39),
AKC 141 (STRUCTURE 40),
AKC 142 (STRUCTURE 41),
AKC 143 (STRUCTURE 42), and
AKC 144 (STRUCTURE 43).

For the foregoing Formulae I, II, III, IV, and V, as well as throughout this disclosure, the following definitions apply.

"Aryl" refers to an aromatic group, typically of 6-10 C atoms, such as phenyl or naphthyl.

"Alk" includes, for example, $(CH_2)_n$ wherein n is an integer of up to 6, *e.g.* 1, 2, 3, or 4, or cyclohexylene.

"Heteroaryl" means an aromatic group including one or more heteroatoms selected from O, S and N. It will typically have 5 or 6 ring atoms. It may also be fused to one or more aryl groups. Examples are in the illustrated compounds.

"Heterocycloalkyl" means a cycloalkyl group in which one or more C atoms are replaced by one or more heteroatoms selected from O, S and N. It will typically have 5 or 6 ring atoms. Examples are in the illustrated compounds of structures 1-43.

Other preferred anthelmintic compounds useful according to the subject invention are represented by structures 44, 45, and 46 (depicted in Figures 44-46, respectively),and have been assigned the respective reference numbers:

AKC 145 (STRUCTURE 44),
AKC 146 (STRUCTURE 45), and
AKC 147 (STRUCTURE 46).

The invention process is particularly valuable to control nematodes which are pests to animals, as well as nematodes attacking the roots of desired crop plants, ornamental plants, and turf grasses. The desired crop plants can be, for example, cotton, soybean, tomatoes, potatoes, grapes, strawberries, bananas, or vegetables.

In one embodiment of the subject invention, the subject anthelmintic compounds are used in conjunction with one or more other nematicidal agents. The other nematicidal agents may be, for example, a biological agent, an avermectin, a milbemycin, or a fatty acid.

In another embodiment, the subject invention further provides methods for killing the eggs of nematodes. Thus, the subject invention further relates to the surprising discovery that certain compounds have ovicidal activity against nematode eggs. Compositions comprising the anthelmintic compounds of the subject invention are particularly useful for preplant applications in nematode-control schemes.

Description of the Drawings

Figure 1 depicts Structure 1 which represents anthelmintic compound AKC 111.

Figure 2 depicts Structure 2 which represents anthelmintic compound AKC 112.

Figure 3 depicts Structure 3 which represents anthelmintic compound AKC 113.

Figure 4 depicts Structure 4 which represents anthelmintic compound AKC 107.

Figure 5 depicts Structure 5 which represents anthelmintic compound AKC 114.

Figure 6 depicts Structure 6 which represents anthelmintic compound AKC 108.

Figure 7 depicts Structure 7 which represents anthelmintic compound AKC 115.

Figure 8 depicts Structure 8 which represents anthelmintic compound AKC 116.

Figure 9 depicts Structure 9 which represents anthelmintic compound AKC 117.

Figure 10 depicts Structure 10 which represents anthelmintic compound AKC 118.

Figure 11 depicts Structure 11 which represents anthelmintic compound AKC 119.

Figure 12 depicts Structure 12 which represents anthelmintic compound AKC 110.

Figure 13 depicts Structure 13 which represents anthelmintic compound AKC 120.

Figure 14 depicts Structure 14 which represents anthelmintic compound AKC 121.

Figure 15 depicts Structure 15 which represents anthelmintic compound AKC 2153.

Figure 16 depicts Structure 16 which represents anthelmintic compound AKC 122.

Figure 17 depicts Structure 17 which represents anthelmintic compound AKC 104.

Figure 18 depicts Structure 18 which represents anthelmintic compound AKC 123.

Figure 19 depicts Structure 19 which represents anthelmintic compound AKC 124.

Figure 20 depicts Structure 20 which represents anthelmintic compound AKC 125.

Figure 21 depicts Structure 21 which represents anthelmintic compound AKC 105.

Figure 22 depicts Structure 22 which represents anthelmintic compound AKC 126.

Figure 23 depicts Structure 23 which represents anthelmintic compound AKC 102.

Figure 24 depicts Structure 24 which represents anthelmintic compound AKC 103.

Figure 25 depicts Structure 25 which represents anthelmintic compound AKC 171.

Figure 26 depicts Structure 26 which represents anthelmintic compound AKC 128.

Figure 27 depicts Structure 27 which represents anthelmintic compound AKC 129.

Figure 28 depicts Structure 28 which represents anthelmintic compound AKC 130.

Figure 29 depicts Structure 29 which represents anthelmintic compound AKC 121.

Figure 30 depicts Structure 30 which represents anthelmintic compound AKC 132.

Figure 31 depicts Structure 31 which represents anthelmintic compound AKC 133.

Figure 32 depicts Structure 32 which represents anthelmintic compound AKC 109.

Figure 33 depicts Structure 33 which represents anthelmintic compound AKC 134.

Figure 34 depicts Structure 34 which represents anthelmintic compound AKC 135.

Figure 35 depicts Structure 35 which represents anthelmintic compound AKC 136.

Figure 36 depicts Structure 36 which represents anthelmintic compound AKC 137.

Figure 37 depicts Structure 37 which represents anthelmintic compound AKC 138.

Figure 38 depicts Structure 38 which represents anthelmintic compound AKC 139.

Figure 39 depicts Structure 39 which represents anthelmintic compound AKC 140.

Figure 40 depicts Structure 40 which represents anthelmintic compound AKC 141.

Figure 41 depicts Structure 41 which represents anthelmintic compound AKC 142.

Figure 42 depicts Structure 42 which represents anthelmintic compound AKC 143.

Figure 43 depicts Structure 43 which represents anthelmintic compound AKC 144.

Figure 44 depicts Structure 44 which represents anthelmintic compound AKC 145.

Figure 45 depicts Structure 45 which represents anthelmintic compound AKC 146.

Figure 46 depicts Structure 46 which represents anthelmintic compound AKC 147.

Figure 47 depicts a basic structure, Structure 47, of a preferred class of anthelmintic compound.

Figure 48 depicts anthelmintic compound AKC 842 of the class represented in Figure 47.

Figure 49 depicts anthelmintic compound AKC 854 of the class represented in Figure 47.

Figure 50 depicts anthelmintic compound AKC 843 of the class represented in Figure 47.

Figure 51 depicts anthelmintic compound AKC 844 of the class represented in Figure 47.

Figure 52 depicts anthelmintic compound AKC 845 of the class represented in Figure 47.

Figure 52 depicts anthelmintic compound AKC 851 of the class represented in Figure 47.

Figure 54 depicts anthelmintic compound AKC 848 of the class represented in Figure 47.

Figure 55 depicts anthelmintic compound AKC 847 of the class represented in Figure 47.

Figure 56 depicts anthelmintic compound AKC 849 of the class represented in Figure 47.

Figure 57 depicts anthelmintic compound AKC 852 of the class represented in Figure 47.

Figure 58 depicts anthelmintic compound AKC 855 of the class represented in Figure 47.

Figure 59 depicts anthelmintic compound AKC 846 of the class represented in Figure 47.

Figure 60 depicts anthelmintic compound AKC 850 of the class represented in Figure 47.

Figure 61 depicts anthelmintic compound AKC 853 of the class represented in Figure 47.

Figure 62 depicts anthelmintic compound AKC 856 of the class represented in Figure 47.

Figure 63 depicts anthelmintic compound AKC 866 of the class represented in Figure 47.

Figure 64 depicts anthelmintic compound AKC 857 of the class represented in Figure 47.

Figure 65 depicts anthelmintic compound AKC 867 of the class represented in Figure 47.

Figure 66 depicts anthelmintic compound AKC 858 of the class represented in Figure 47.

Figure 67 depicts anthelmintic compound AKC 864 of the class represented in Figure 47.

Figure 68 depicts anthelmintic compound AKC 868 of the class represented in Figure 47.

Figure 69 depicts anthelmintic compound AKC 870 of the class represented in Figure 47.

Figure 70 depicts anthelmintic compound AKC 859 of the class represented in Figure 47.

Figure 71 depicts anthelmintic compound AKC 862 of the class represented in Figure 47.

Figure 72 depicts anthelmintic compound AKC 869 of the class represented in Figure 47.

Figure 73 depicts anthelmintic compound AKC 860 of the class represented in Figure 47.

Figure 74 depicts anthelmintic compound AKC 865 of the class represented in Figure 47.

Figure 75 depicts anthelmintic compound AKC 861 of the class represented in Figure 47.

Figure 76 depicts anthelmintic compound AKC 863 of the class represented in Figure 47.

Figure 77 depicts anthelmintic compound AKC 872 of the class represented in Figure 47.

Figure 78 depicts anthelmintic compound AKC 876 of the class represented in Figure 47.

Figure 79 depicts anthelmintic compound AKC 878 of the class represented in Figure 47.

Figure 80 depicts anthelmintic compound AKC 871 of the class represented in Figure 47.

Figure 81 depicts anthelmintic compound AKC 880 of the class represented in Figure 47.

Figure 82 depicts anthelmintic compound AKC 873 of the class represented in Figure 47.

Figure 83 depicts anthelmintic compound AKC 879 of the class represented in Figure 47.

Figure 84 depicts anthelmintic compound AKC 881 of the class represented in Figure 47.

Figure 85 depicts anthelmintic compound AKC 874 of the class represented in Figure 47.

Figure 86 depicts anthelmintic compound AKC 877 of the class represented in Figure 47.

Figure 87 depicts anthelmintic compound AKC 875 of the class represented in Figure 47.

Figure 88 depicts anthelmintic compound AKC 882 of the class represented in Figure 47.

Figure 89 depicts anthelmintic compound AKC 884 of the class represented in Figure 47.

Figure 90 depicts anthelmintic compound AKC 883 of the class represented in Figure 47.

Figure 91 depicts anthelmintic compound AKC 885 of the class represented in Figure 47.

Figure 92 depicts anthelmintic compound AKC 886 of the class represented in Figure 47.

Figure 93 depicts anthelmintic compound AKC 896 of the class represented in Figure 47.

Figure 94 depicts anthelmintic compound AKC 888 of the class represented in Figure 47.

Figure 95 depicts anthelmintic compound AKC 890 of the class represented in Figure 47.

Figure 96 depicts anthelmintic compound AKC 894 of the class represented in Figure 47.

Figure 97 depicts anthelmintic compound AKC 897 of the class represented in Figure 47.

Figure 98 depicts anthelmintic compound AKC 889 of the class represented in Figure 47.

Figure 99 depicts anthelmintic compound AKC 891 of the class represented in Figure 47.

Figure 100 depicts anthelmintic compound AKC 895 of the class represented in Figure 47.

Figure 101 depicts anthelmintic compound AKC 898 of the class represented in Figure 47.

Figure 102 depicts anthelmintic compound AKC 887 of the class represented in Figure 47.

Figure 103 depicts anthelmintic compound AKC 892 of the class represented in Figure 47

Figure 104 depicts anthelmintic compound AKC 893 of the class represented in Figure 47.

Figure 105 depicts anthelmintic compound AKC 899 of the class represented in Figure 47.

Figure 106 depicts anthelmintic compound AKC 900 of the class represented in Figure 47.

Figure 107 depicts anthelmintic compound AKC 907 of the class represented in Figure 47.

Figure 108 depicts anthelmintic compound AKC 902 of the class represented in Figure 47.

Figure 109 depicts anthelmintic compound AKC 908 of the class represented in Figure 47.

Figure 110 depicts anthelmintic compound AKC 903 of the class represented in Figure 47.

Figure 111 depicts anthelmintic compound AKC 906 of the class represented in Figure 47.

Figure 112 depicts anthelmintic compound AKC 909 of the class represented in Figure 47.

Figure 113 depicts anthelmintic compound AKC 910 of the class represented in Figure 47.

Figure 114 depicts anthelmintic compound AKC 901 of the class represented in Figure 47.

Figure 115 depicts anthelmintic compound AKC 904 of the class represented in Figure 47.

Figure 116 depicts anthelmintic compound AKC 905 of the class represented in Figure 47.

Figure 117 depicts anthelmintic compound AKC 811 of the class represented in Figure 47.

Figure 118 depicts anthelmintic compound AKC 810 of the class represented in Figure 47.

Figure 119 depicts anthelmintic compound AKC 911 of the class represented in Figure 47.

Figure 120 depicts anthelmintic compound AKC 912 of the class represented in Figure 47.

Figure 121 depicts anthelmintic compound AKC 913 of the class represented in Figure 47.

Figure 122 depicts anthelmintic compound AKC 914 of the class represented in Figure 47.

Figure 123 depicts anthelmintic compound AKC 916 of the class represented in Figure 47.

Figure 124 depicts anthelmintic compound AKC 918 of the class represented in Figure 47.

Figure 125 depicts anthelmintic compound AKC 920 of the class represented in Figure 47.

Figure 126 depicts anthelmintic compound AKC 919 of the class represented in Figure 47.

Figure 127 depicts anthelmintic compound AKC 922 of the class represented in Figure 47.

Figure 128 depicts anthelmintic compound AKC 923 of the class represented in Figure 47.

Figure 129 depicts anthelmintic compound AKC 915 of the class represented in Figure 47.

Figure 130 depicts anthelmintic compound AKC 917 of the class represented in Figure 47.

Figure 131 depicts anthelmintic compound AKC 921 of the class represented in Figure 47.

Figure 132 depicts anthelmintic compound AKC 924 of the class represented in Figure 47.

Figure 133 depicts anthelmintic compound AKC 925 of the class represented in Figure 47.

Figure 134 depicts anthelmintic compound AKC 926 of the class represented in Figure 47.

Figure 135 depicts anthelmintic compound AKC 927 of the class represented in Figure 47.

Figure 136 depicts anthelmintic compound AKC 928 of the class represented in Figure 47.

Figure 137 depicts anthelmintic compound AKC 929 of the class represented in Figure 47.

Figure 138 depicts anthelmintic compound AKC 930 of the class represented in Figure 47.

Figure 139 depicts anthelmintic compound AKC 932 of the class represented in Figure 47.

Figure 140 depicts anthelmintic compound AKC 935 of the class represented in Figure 47.

Figure 141 depicts anthelmintic compound AKC 933 of the class represented in Figure 47.

Figure 142 depicts anthelmintic compound AKC 936 of the class represented in Figure 47.

Figure 143 depicts anthelmintic compound AKC 931 of the class represented in Figure 47.

Figure 144 depicts anthelmintic compound AKC 934 of the class represented in Figure 47.

Figure 145 depicts anthelmintic compound AKC 937 of the class represented in Figure 47.

Figure 146 depicts anthelmintic compound AKC 812 of the class represented in Figure 47.

Figure 147 depicts anthelmintic compound AKC 938 of the class represented in Figure 47.

Figure 148 depicts anthelmintic compound AKC 939 of the class represented in Figure 47.

Figure 149 depicts anthelmintic compound AKC 941 of the class represented in Figure 47.

Figure 150 depicts anthelmintic compound AKC 940 of the class represented in Figure 47.

Figure 151 depicts anthelmintic compound AKC 942 of the class represented in Figure 47.

Figure 152 depicts anthelmintic compound AKC 945 of the class represented in Figure 47.

Figure 153 depicts anthelmintic compound AKC 943 of the class represented in Figure 47.

Figure 154 depicts anthelmintic compound AKC 946 of the class represented in Figure 47.

Figure 155 depicts anthelmintic compound AKC 948 of the class represented in Figure 47.

Figure 156 depicts anthelmintic compound AKC 103 of the class represented in Figure 47.

Figure 157 depicts anthelmintic compound AKC 949 of the class represented in Figure 47.

Figure 158 depicts anthelmintic compound AKC 944 of the class represented in Figure 47.

Figure 159 depicts anthelmintic compound AKC 947 of the class represented in Figure 47.

Figure 160 depicts anthelmintic compound AKC 950 of the class represented in Figure 47.

Figure 161 depicts anthelmintic compound AKC 951 of the class represented in Figure 47.

Figure 162 depicts anthelmintic compound AKC 954 of the class represented in Figure 47.

Figure 163 depicts anthelmintic compound AKC 952 of the class represented in Figure 47.

Figure 164 depicts anthelmintic compound AKC 953 of the class represented in Figure 47.

Figure 165 depicts anthelmintic compound AKC 959 of the class represented in Figure 47.

Figure 166 depicts anthelmintic compound AKC 956 of the class represented in Figure 47.

Figure 167 depicts anthelmintic compound AKC 957 of the class represented in Figure 47.

Figure 168 depicts anthelmintic compound AKC 955 of the class represented in Figure 47.

Figure 169 depicts anthelmintic compound AKC 958 of the class represented in Figure 47.

Figure 170 depicts anthelmintic compound AKC 960 of the class represented in Figure 47.

Figure 171 depicts anthelmintic compound AKC 818 of the class represented in Figure 47.

Figure 172 depicts anthelmintic compound AKC 815 of the class represented in Figure 47.

Figure 173 depicts anthelmintic compound AKC 813 of the class represented in Figure 47.

Figure 174 depicts anthelmintic compound AKC 814 of the class represented in Figure 47.

Figure 175 depicts anthelmintic compound AKC 816 of the class represented in Figure 47.

Figure 176 depicts anthelmintic compound AKC 817 of the class represented in Figure 47.

Figure 177 depicts anthelmintic compound AKC 819 of the class represented in Figure 47.

Figure 178 depicts anthelmintic compound AKC 963 of the class represented in Figure 47.

Figure 179 depicts anthelmintic compound AKC 962 of the class represented in Figure 47.

Figure 180 depicts anthelmintic compound AKC 961 of the class represented in Figure 47.

Figure 181 depicts anthelmintic compound AKC 964 of the class represented in Figure 47.

Figure 182 depicts anthelmintic compound AKC 966 of the class represented in Figure 47.

Figure 183 depicts anthelmintic compound AKC 965 of the class represented in Figure 47.

Figure 184 depicts anthelmintic compound AKC 969 of the class represented in Figure 47.

Figure 185 depicts anthelmintic compound AKC 968 of the class represented in Figure 47.

Figure 186 depicts anthelmintic compound AKC 970 of the class represented in Figure 47.

Figure 187 depicts anthelmintic compound AKC 967 of the class represented in Figure 47.

Figure 188 depicts anthelmintic compound AKC 971 of the class represented in Figure 47.

Figure 189 depicts anthelmintic compound AKC 972 of the class represented in Figure 47.

Figure 190 depicts anthelmintic compound AKC 973 of the class represented in Figure 47.

Figure 191 depicts anthelmintic compound AKC 820 of the class represented in Figure 47.

Figure 192 depicts anthelmintic compound AKC 821 of the class represented in Figure 47.

Figure 193 depicts anthelmintic compound AKC 822 of the class represented in Figure 47.

Figure 194 depicts anthelmintic compound AKC 974 of the class represented in Figure 47.

Figure 195 depicts anthelmintic compound AKC 975 of the class represented in Figure 47.

Figure 196 depicts anthelmintic compound AKC 976 of the class represented in Figure 47.

Figure 197 depicts anthelmintic compound AKC 978 of the class represented in Figure 47.

Figure 198 depicts anthelmintic compound AKC 977 of the class represented in Figure 47.

Figure 199 depicts anthelmintic compound AKC 979 of the class represented in Figure 47.

Figure 200 depicts anthelmintic compound AKC 980 of the class represented in Figure 47.

Figure 201 depicts anthelmintic compound AKC 981 of the class represented in Figure 47.

Figure 202 depicts anthelmintic compound AKC 982 of the class represented in Figure 47.

Figure 203 depicts anthelmintic compound AKC 983 of the class represented in Figure 47.

Figure 204 depicts anthelmintic compound AKC 986 of the class represented in Figure 47.

Figure 205 depicts anthelmintic compound AKC 984 of the class represented in Figure 47.

Figure 206 depicts anthelmintic compound AKC 985 of the class represented in Figure 47.

Figure 207 depicts anthelmintic compound AKC 987 of the class represented in Figure 47.

Figure 208 depicts anthelmintic compound AKC 823 of the class represented in Figure 47.

Figure 209 depicts anthelmintic compound AKC 824 of the class represented in Figure 47.

Figure 210 depicts anthelmintic compound AKC 830 of the class represented in Figure 47.

Figure 211 depicts anthelmintic compound AKC 828 of the class represented in Figure 47.

Figure 212 depicts anthelmintic compound AKC 825 of the class represented in Figure 47.

Figure 213 depicts anthelmintic compound AKC 831 of the class represented in Figure 47

Figure 214 depicts anthelmintic compound AKC 832 of the class represented in Figure 47.

Figure 215 depicts anthelmintic compound AKC 826 of the class represented in Figure 47.

Figure 216 depicts anthelmintic compound AKC 827 of the class represented in Figure 47.

Figure 217 depicts anthelmintic compound AKC 829 of the class represented in Figure 47.

Figure 218 depicts anthelmintic compound AKC 833 of the class represented in Figure 47.

Figure 219 depicts anthelmintic compound AKC 834 of the class represented in Figure 47.

Figure 220 depicts anthelmintic compound AKC 835 of the class represented in Figure 47.

Figure 221 depicts anthelmintic compound AKC 836 of the class represented in Figure 47.

Figure 222 depicts anthelmintic compound AKC 840 of the class represented in Figure 47.

Figure 223 depicts anthelmintic compound AKC 837 of the class represented in Figure 47.

Figure 224 depicts anthelmintic compound AKC 841 of the class represented in Figure 47.

Figure 225 depicts anthelmintic compound AKC 838 of the class represented in Figure 47.

Figure 226 depicts anthelmintic compound AKC 839 of the class represented in Figure 47.

Figure 227 depicts one library scheme by which the skilled artisan can create the compounds represented by the structure depicted in Figure 47.

Figure 228 depicts hydroxamidine synthesized from a benzonitrile and hydroxylamine hydrochloride.

Figure 229 depicts a BOC-amino acid prepared by catalytic hydrogenation of a pyridine-containing acid and subsequent BOC-protection.

Detailed Disclosure of the Invention

The process of the subject invention concerns the use of certain organic compounds to control the infestation of plants or animals by nematodes. These organic compounds comprise Formulae I, II, III, IV, and V, as well as Structures 44, 45, and 46. In a particularly preferred embodiment of the subject invention, the anthelmintic compound is selected from the group consisting of Compounds 1-46 represented by Structures 1-46. Particularly preferred is the compound represented by Structure 24, and compounds related thereto as represented by Structure 47 depicted in Figure 47, and as further exemplified by Structures 48-226 depicted in Figures 48 through 226. Preferred anthelmintic compounds useful in accord with the subject invention are represented by Structure 47, wherein:

R_1 is C_{1-5} straight or branched alkyl; OC_{1-5}; or SO_2C_{1-5};

R_2 is C_{1-5} alkyl; OC_{1-5}; or SO_2C_{1-5};

or R_1 and R_2 form a 5 member acetal group;

R_3 is CH_2Ar (with the aryl optionally substituted with C_{1-5} alkyl); heterocycle (optionally substituted with C_{1-5} alkyl); or C_{3-8} cyclic alkyl;

R_4 is C_{1-10} straight or branched alkyl (optionally substituted with phenyl);

R_5 is CSAr; aryl (optionally substituted with C_{1-5} straight or branched alkyl; OC_{1-5}, halogen, or NO_2); heteroaryl (optionally substituted with halogen); C_{1-5} straight or branched alkyl which is optionally substituted with aryl (optionally substituted with OC_{1-5} or an acetal group); CH_2ArNO_2; naphthyl (optionally substituted with OC); C_{3-5} cycloalkyl which is optionally substituted with aryl (optionally substituted with halogen); CH_2OR_6 wherein R_6 is C_{3-8} cycloalkyl (optionally substituted with C_{1-5} straight or branched alkyl);

or R_3 and R_4 form a heterocycle which is optionally substituted with a C_{1-5} alkyl which is then connected to the core structure heterocycle (oxaimidazole).

Generally, the anthelmintic compounds of the subject invention can be unsubstituted or substituted, saturated or unsaturated. The anthelmintic component of an anthelmintic composition used according to the subject invention may be a single

anthelmintic compound or a mixture of two or more anthelmintic compounds. The subject compounds may be used in conjunction with other anthelmintic compounds, including the free acids and salts of the anthelmintic compounds of the present invention. The salts may be, for example, sodium or potassium salts, or ammonium salts. As would be apparent to the ordinary skilled artisan, physiologically acceptable acids and salts of the subject anthelmintic compounds can readily be made and used in accord with the teachings herein, and are hereby expressly included by reference to each compound or group of compounds. For example, "AKC 842", "Compound 48", or "Structure 48" each refer to the same compounds and each is intended to include the physiologically acceptable acids and salts thereof. In addition, the subject anthelmintic compounds may have an assymetrical carbon atom, *i.e.*, optically active site. These compounds exist in (R) and (S) enantiomeric forms. Both the (R) and (S) enantiomers of the subject compounds are contemplated by the subject invention.

Anthelmintic compounds specifically exemplified herein include Compounds 1-46 represented by Structures 1-46 above, and Compounds 48-226 represented by Structures 48-226 depicted in Figures 48-226.

The subject compounds used in the invention can be applied to animals, the living and feeding areas of animals, plants, or to the situs of plants needing nematode control. The anthelmintic compositions may be applied by, for example, drip and drench techniques. With the drip application, the subject compositions can be applied directly to the base of plants or to the soil root zone. The composition may be applied through already existing drip irrigation systems. This procedure is particularly applicable for ornamental plants, strawberries, tomatoes, potatoes, grapes, and vegetables. Alternatively, a drench application can be used. For treating plants, a sufficient quantity of the anthelmintic composition is applied such that the composition drains to the root area of the plants. An important aspect of the subject invention is the surprising discovery that certain compounds have excellent nematicidal activity at concentrations which are not phytotoxic.

The drench technique can be used for a variety of crops and for turf grasses. The drench technique can also be used for animals. Preferably, for administration to animals the anthelmintic composition would be administered orally to facilitate activity against

internal nematode parasites. The compositions of the subject invention can readily be applied using the teachings provided herein.

In a preferred embodiment of the subject invention, an anthelmintic compound will be applied as an aqueous microemulsion. As described herein, the concentration of the active ingredient should be sufficient to control the nematode infestation without causing phytotoxicity to the desired plants. The concentration of anthelmintic compound may be, for example, from about 0.0001% to about 2%, preferably from about 0.025% to about 1%, and, most preferably, from about 0.05% to about 0.5%.

The anthelmintic composition used according to the subject invention can be applied in conjunction with one or more other nematicidal agents. The other nematicidal agent may, for example, be applied simultaneously or sequentially with the anthelmintic. Such other nematicidal agents include, for example, avermectins, the *B.t.*s, and fatty acids.

The avermectin compound used according to the subject invention may be any of the avermectins, milbemycins, or derivatives of either, having activity against nematodes. The avermectin's activity will be enhanced when combined with an anthelmintic compound as described herein. Thus, the specific combination of ingredients can be manipulated to provide the optimal composition for a particular application.

Standard concentrations of avermectins are well known to those skilled in the art. For example, the avermectin compounds can be employed in the combination of the subject invention at concentrations of from about 0.03 to about 110 parts per million (ppm). Preferably, from about 1 to about 5 ppm are employed.

As would be readily appreciated by a person skilled in the art, the delivery of the subject anthelmintic and/or avermectin compound can be calculated in terms of the active ingredient applied per unit area. For example, the subject anthelmintic may be applied at a rate of about 0.02 lb/acre to about 0.1 lb/acre and, preferably, from about 0.5 lb/acre to about 2 lbs/acre. Similarly, the avermectin product can be applied at a rate of up to about 16 oz. of formulated product ("AVID," available from Merck) per acre. Preferably, about 4 oz. to about 8 oz. formulated "AVID" per acre would be used. Thus, the avermectin compound can be applied up to about 0.02 lb/acre. Preferably, the rate of avermectin is between about 0.005 lb/acre and 0.01 lb/acre. A person of ordinary skill in the art would readily appreciate that the desired application rate of the active ingredients could be achieved using a great variety of different concentrations of active ingredients while

varying the application rate of the solution. Thus, a large quantity of dilute solution could be applied or a smaller quantity of a more concentrated solution.

A variety of different avermectins or related compounds can be used according to the subject invention. Ivermectin may also be used according to the subject invention, as may the milbemycins. For brevity, the term "avermectin" is used herein to refer to all the avermectins and their derivatives as well as related compounds such as the milbemycins and the ivermectins. "Derivatives" refer to chemical modifications of the avermectins or milbemycins which are well known and available to those skilled in this art. Such derivatives are described, for example, in U.S. Patent No. 4,560,677. Avermectin is readily available under a variety of tradenames including "AVID," "ZEPHYR," "VERTIMEC," and "AGRI-MEK."

The anthelmintic compositions of the subject invention may also be used in conjunction with nematicidal agents other than the avermectins. For example, the anthelmintic compounds may be used with biological agents such as *Bacillus thuringiensis* or with nematicidal fungi. In this context, the anthelmintic composition could be applied at concentrations which would not antagonize the action of the biological agent. The biologically active agent may be in a live proliferative form or may be in a dead stabilized form as described, for example, in U.S. Patent Nos. 4,695,462 and 4,695,455. Furthermore, the anthelmintic compositions of the subject invention may be used with plants which are specifically bred or engineered for nematode resistance. The plants may, for example, be transformed with *B.t.* genes which confer nematode resistance or may simply be hybrids or varieties selected for such resistance. The anthelmintic compositions of the subject invention are particularly effective against free-living ectoparasitic nematodes and, therefore, combined use with plants selected for endoparasitic nematode resistance is highly advantageous.

The subject invention further relates to the surprising discovery that the anthelmintics of the subject invention have ovicidal activity against nematode eggs. Thus, in another embodiment, provided are methods for killing the eggs of nematodes, including those within cysts or egg masses that are commonly formed by *Heterodera, Globodera,* and *Meloidogyne* (cyst and root-knot) species.

The ovicidal compositions according to the subject invention are particularly useful for preplant applications in nematode-control schemes. In addition, the ovicidal

compositions of the subject invention can be advantageously used as postplant nematicides, especially because of their relatively low phytotoxicity. In the latter embodiments, ovicidal compositions of the subject invention can be delivered, after planting and at appropriate, essentially non-phytotoxic concentrations of anthelmintic compounds, along with irrigation water and/or plant nutrients to ensure a continuous zone of nematode protection to the enlarging plant root mass. Thus, when applied using these techniques, which include drench or drip systems as are known in the art, phytopathogenic nematodes in their vermiform (wormlike) and egg stages are controlled.

Anthelmintic compounds having Formulae I, II, III, IV, and V, Structure 47, and most preferably Structures 1-46, and particularly Structure 24 and Structures 48-226 are used in preferred embodiments for killing nematode eggs. In addition, microemulsions of the subject compounds are highly preferred for ovicidal applications. In preferred embodiments, the anthelmintic compound(s) will be present in a concentration of greater than about 150 ppm. More preferably, the concentration will be greater than about 200 ppm; most preferably it will be about 250 ppm or more. For certain conditions, the anthelmintic compounds should be applied at high concentrations of about 1,000 ppm to about 5,000 ppm or more.

In light of the subject disclosure, one skilled in the art could readily use a variety of application techniques and formulations to prevent the hatching of nematode eggs in a variety of agricultural, farm-related, and garden-related settings.

Examples of animal parasitic nematodes against which the subject compounds can be used include the following:

Amblyomma spp.
Babesia spp. (RBC)
Bunostomum spp.
Calliphorid larvae
Capillaria spp.
Chabertia ovina
Chorioptes
Cooperia spp.
Cryptosporidium sp.
Damalinia ovis
Damalinia caprae
Demodex
Dermacentor spp.
Dicrocoelium dentriticum

Dictyocaulus filaria
Echinococcus hydatid cyst
Eimeria spp.
Elaeophora schneideri
Fasciola hepatica
Fasciola gigantica
Fascioloides magna
Giardia sp.
Gongylonema spp.
Haematobia irritans
Haemonchus contortus contortus
Ixodes
Linguatula serrata larvae
Linguatula serrata nymphs
Linognathus spp.
M. domestica
Marshallagia marshalli
Melophagus ovinus
Moniezia benedeni
Moniezia expansa
Muellerius capillaris
Musca autumnalis
Nematodirus spp.
Oesophagostomum spp.
Oestrus ovis
Ornithodoros
Ostertagia circumcincta
Ostertagia trifurcata
Otobius
Paramphistomum sp.
Parelaphostrongylus tenuis
Protostrongylus sp.
Psoroptes
Rhipicephalus spp.
Sarcoptes scabiei
Sarcocystis spp.
Sarcocystis spp. cysts
Schistosoma spp.
Stomoxys calcitrans
Strongyloides papillosus
Taenia hydatigena cysticerci
Taenia multiceps coenurus
Taenia ovis cysticerci
Thelazia
Thysanosoma actinoides
Theileria spp.C)
Toxocara vitulorum
Toxoplasma gondii

Toxoplasma gondii cysts
Trichostrongylus axei
Trichostrongylus spp.
Trichuris ovis
Trypanosoma spp. (plasma)

It has been found that helminth, acarid and arthropod endo- and ectoparasitic infestations may be controlled, prevented or eliminated, by applying to, injecting or orally dosing said animals with an endo- or ectoparasiticidally effective amount of the subject anthelmintic compounds, preferably the above-described Structure 1-46 and 48-226 compounds. This may be achieved by applying the compound to the skin, hide and/or hair of the animals, or injecting or orally dosing said animals with a solid or liquid formulated composition.

For control of flea infestations, treatment of the infested animal to control adults in conjunction with treatment of the area occupied by the infested animal to control flea larvae is recommended. The compositions of the present invention may be admixed with suitable carriers for application to interior and/or exterior areas for control of flea larvae.

The compositions of the present invention may be employed as animal feeds, animal feed premixes or feed concentrates. Feed concentrates and feed premixes, useful in the practice of the invention, may be prepared by admixing about 0.25% to 35% by weight of a subject anthelmintic compound, preferably a Structure 1-46 or 48-226 compound, with about 99.75% to 65% by weight of a suitable agronomic carrier or diluent. Carriers suitable for use include 0.75% to 35% by weight of a physiologically acceptable alcohol such as benzyl alcohol, phenethyl alcohol or propylene glycol, 0 to about 10% by weight of a vegetable oil such as corn oil or soybean oil, or propylene glycol and about 30% to 95% by weight of a sorptive, edible organic carrier such as corn grits, wheat middlings, soybean meal, expanded corn grits, extracted corn meal or the like or a sorptive silica or a silicate. These feed premixes or concentrates may be admixed with the appropriate amount of animal feed to provide the animals with about 0.5 ppm to 1,000 ppm and preferably about 1 ppm to 500 ppm of the compound in the animal's diet. These premixes or concentrates may also be used as top dressings for the animal's daily ration and applied across the top of the daily ration in sufficient amount to provide the animal with about 0.5 ppm to 1,000 ppm and preferably about 1 ppm to 500 ppm of the active ingredient, based on the animal's total feed.

The subject anthelmintic compounds, and particularly the Structure 1-46 compounds, most particularly Structure 24 and Structures 48-226 compounds, may be administered to the animals in or with their drinking water.

The compound may also be administered in the form of a pill, tablet, bolus, implant, capsule, or drench, containing sufficient anthelmintic compound to provide the treated animal with about 0.01 mg/kg to 100 mg/kg of animal body weight per day of the compound. These dosage forms are prepared by intimately and uniformly mixing the active ingredient with suitable finely divided diluents, fillers, disintegrating agents and/or builders such as starch, lactose, talc, magnesium stearate, vegetable gums, or the like. These unit dosage formulations may be varied with respect to the total weight and content of anthelmintic compound depending upon the kind and size of the animal to be treated, the severity or type of infection encountered and the weight of the host.

Alternatively, the anthelmintic compound may be administered to animals parenterally, for example, by intraruminal, intramuscular, or subcutaneous injection in which the active ingredient is dissolved or dispersed in a liquid carrier. For this type administration the compound may be dispersed in a physiologically acceptable solvent for subcutaneous injection, or it may be dispersed in a fat or wax or mixture thereof containing an oil, buffer, surfactant, stabilizer, preservative and salt. Components useful in these preparations include carbowax, aluminum monostearate gel, diethyl succinate, soya oil, glyceral dioleate, saline, and capric/caprylic triglycerides.

The subject anthelmintic compounds may also be applied topically to the larger animals such as swine, sheep, cattle, and horses and companion animals such as dogs and cats in the form of aqueous dips or sprays. For this type administration, the active compound is generally prepared as a wettable powder, emulsifiable concentrate, aqueous flowable, or the like, which is mixed with water at the site of treatment and applied topically to the hide, skin, or hair of the animal. Such sprays or dips usually contain about 0.5 ppm to 5,000 ppm and preferably about 1 ppm to 3,000 ppm of the compound.

Advantageously, the subject anthelmintic compounds may also be prepared as pour-on formulations and poured on the backs of the animals such as swine, cattle, sheep, horses, poultry, and companion animals to protect them against infestation by nematodes, acarids, and arthropod endo- and ectoparasites. Such pour-on compositions are generally prepared by dissolving, dispersing, or emulsifying the anthelmintic compound in a suitable

nontoxic pharmacologically acceptable diluent for pour-on and administration. The diluent must be compatible with the compound and should not be a source of irritation or damage to the animals hide, skin, or hair. Such diluents include vegetable oils, spreading oils, polyhydric alcohols, aliphatic or aromatic hydrocarbons, esters of fatty acids, and lower alkyl ketones.

A typical pour-on formulation includes about 0.5% to 30% by weight of the anthelmintic compound, about 30% to 60% by weight of an aliphatic or aromatic hydrocarbon, mono or polyhydric alcohol, lower alkyl ketone or mixtures thereof, 0 to about 20% by weight of a vegetable or mineral oil and about 0.5% to 30% by weight of a spreading oil. Another typical pour-on contains about 45% by weight of xylene, about 15% by weight of the anthelmintic compound, about 10% by weight of corn oil or mineral oil, about 25% by weight of cyclohexanone and about 5% by weight of other pharmacologically acceptable spreading agents, antifoam agents, surfactants, or the like.

The subject anthelmintic compounds may also be prepared as ear tags for animals, particularly quadrupeds such as cattle and sheep. The tags may be prepared by stirring together about 55% to 60% by weight of a vinyl dispersion resin, having an inherent viscosity of about 1.20 and an average particle size of about 0.75 microns, a curing temperature range of about 120°C to 180°C, with about 28% by weight of butylbenzylphthalate. Stirring is continued, and about 1.5% by weight of ca/Zn stearate stabilizer is added along with about 7.0% of the compound and 2.8% of epoxidized soybean oil. The resulting mixture is deaerated for 15 to 20 minutes at 125 mm/Hg. This mixture can be coated on an ear tag blank by dipping and the resulting tag cured at about 145°C to 150°C for about five minutes.

The compounds of Formulae I-V, Structure 47, particularly Structures 1-46, and particularly Structures 24 and 48-226 are nematicidal and can be used to control nematodes in crop plants. Therefore, in a further preferred aspect of the invention, there is provided a method for killing or controlling nematodes which comprises applying to the locus of the pests or to a plant susceptible to attack by the pest an effective amount of a compound having any of Structures 1-46, preferably Structure 47, and particularly Structures 24 and 48-226, as defined herein.

The term "controlling" extends to non-lethal effects which result in the reduction or prevention of damage to the host plant or animal and the limitation of nematode

population increase. These effects may be the result of chemical induced disorientation, immobilisation, or hatch prevention or induction. The chemical treatment may also have deleterious effects on nematode development, reproduction, or viability.

The compounds of the invention can be used against both plant-parasitic nematodes and nematodes living freely in the soil. Examples of plant-parasitic nematodes are: ectoparasites, for example Xiphinema spp., Longidorus spp., and Trichodorous spp.; semi-endoparasites, for example, Tylenchulus spp.; migratory endoparasites, for example, Pratylenchus spp., Radopholus spp., and Scutellonema spp.; sedentary endoparasites, for example, Heterodera spp., Globodera spp., and Meloidogyne spp.; and stem and leaf endoparasites, for example, Ditylenchus spp., Aphelenchoides spp., and Hirshmaniella spp..

The Formulae I-V compounds, Structure 47 compounds, and preferably the compounds of Structures 1-46, more preferably the compounds of Structures 24 and 48-226, display nematicidal activity against different types of nematodes including the cyst nematode. The subject compounds may also be used to combat and control infestations of insect pests such as Lepidoptera, Diptera, Homoptera, and Coleoptera (including Diabrotica i.e. corn rootworms) and also other invertebrate pests, for example, acarine pests. The insect and acarine pests which may be combated and controlled by the use of the invention compounds include those pests associated with agriculture (which term includes the growing of crops for food and fiber products), horticulture and animal husbandry, forestry, the storage of products of vegetable origin, such as fruit, grain and timber, and also those pests associated with the transmission of diseases of man and animals. Examples of insect and acarine pest species which may be controlled by the subject compounds include:

Myzus persicae (aphid)
Aphis gossypii (aphid)
Aphis fabae (aphid)
Megoura viceae (aphid)
Aedes aegypti (mosquito)
Anopheles spp. (mosquitos)
Culex spp. (mosquitos)
Dysdercus fasciatus (capsid)
Musca domestica (housefly)
Pieris brassicae (white butterfly)
Plutella maculipennis (diamond back moth)
Phaedon cochleariae (mustard beetle)

Aonidiella spp. (scale insects)
Trialeuroides spp. (white flies)
Bemisia tabaci (white fly)
Blattella germanica (cockroach)
Periplaneta americana (cockroach)
Blatta orientalis (cockroach)
Spodoptera littoralis (cotton leafworm)
Hellothis virescens (tobacco budworm)
Chortiocetes terminifera (locust)
Diabrotica spp. (rootworms)
Agrotis spp. (cutworms)
Chilo partellus (maize stem borer)
Nilaparvata lugens (planthopper)
Nephotettix cincticeps (leafhopper)
Panonychus ulmi (European red mite)
Panonychus citri (citrus red mite)
Tetranychus urticae (two-spotted spider mite)
Tetranychus cinnabarinus (carmine spider mite)
Phyllcoptruta oleivora (citrus rust mite)
Polyphagotarsonemus latus (broad mite)
Brevipalpus spp. (mites)

In order to apply the compound to the locus of the nematode, insect, or acarid pest, or to a plant susceptible to attack by the nematode, insect, or acarid pest, the compound is usually formulated into a composition which includes in addition to at least one of the subject anthelmintic compounds suitable inert diluent or carrier materials, and/or surface active agents. Thus, in two further aspects of the invention there is provided a nematicidal, insecticidal, or acaricidal composition comprising an effective amount of a subject anthelmintic compound and preferably of any of Structures 1-46, preferably compounds of Structure 47, more preferably as exemplified by Structures 24 and 48-226, as defined herein and an inert diluent or carrier material and optionally a surface active agent.

The amount of active ingredient generally applied for the control of nematode pests is from 0.01 to 10 kg per hectare, and preferably from 0.1 to 6 kg per hectare.

The compositions containing the active ingredient can be applied to the soil, plant or seed, to the locus of the pests, or to the habitat of the pests, in the form of dusting powders, wettable powders, granules (slow or fast release), emulsion or suspension concentrates, liquid solutions, emulsions, seed dressings, fogging/smoke formulations or controlled release compositions, such as microencapsulated granules or suspensions.

Dusting powders are formulated by mixing the active ingredient with one or more finely divided solid carriers and/or diluents, for example natural clays, kaolin, pyrophyllite, bentonire, alumina, montmorillonite, kieselguhr, chalk, diatomaceous earths, calcium phosphates, calcium and magnesium carbonates, sulphur, lime, flours, talc, and other organic and inorganic solid carriers.

Granules are formed either by absorbing the active ingredient in a porous granular material for example pumice, attapulgite clays, fullers earth, kieselguhr, diatomaceous earths, ground corn cobs, and the like, or on to hard core materials such as sands, silicates, mineral carbonates, sulphates, phosphates, or the like. Agents which are commonly used to aid in impregnation, binding or coating the solid carriers include aliphatic and aromatic petroleum solvents, alcohols, polyvinyl acetates, polyvinyl alcohols, ethers, ketones, esters, dextrins, sugars, and vegetable oils with the active ingredient. Other additives may also be included, such as emulsifying agents, wetting agents, or dispersing agents.

Microencapsulated formulations (microcapsule suspensions CS) or other controlled release formulations may also be used, particularly for slow release over a period of time, and for seed treatment.

Alternatively the compositions may be in the form of liquid preparations to be used as dips, irrigation additives or sprays, which are generally aqueous dispersions or emulsions of the active ingredient in the presence of one or more known wetting agents, dispersing agents or emulsifying agents (surface active agents). The compositions which are to be used in the form of aqueous dispersions or emulsions are generally supplied in the form of an emulsifiable concentrate (EC) or a suspension concentrate (SC) containing a high proportion of the active ingredient or ingredients. An EC is a homogeneous liquid composition, usually containing the active ingredient dissolved in a substantially non-volatile organic solvent. An SC is a fine particle size dispersion of solid active ingredient in water. To apply the concentrates they are diluted in water and are usually applied by means of a spray to the area to be treated. For agricultural or horticultural purposes, an aqueous preparation containing between 0.0001% and 0.1% by weight of the active ingredient (approximately equivalent to from 5-2000 g/ha) is particularly useful.

Suitable liquid solvents for ECs include methyl ketone, methyl isobutyl ketone, cyclohexanone, xylenes, toluene, chlorobenzene, paraffins, kerosene, white oil, alcohols,

(for example, butanol), methylnaphthalene, trimethylbenzene, trichloroethylene, N-methyl-2-pyrrolidone, and tetrahydrofurfuryl alcohol (THFA).

Wetting agents, dispersing agents, and emulsifying agents may be of the cationic, anionic, or non-ionic type. Suitable agents of the cationic type include, for example, quaternary ammonium compounds, for example cetyltrimethyl ammonium bromide. Suitable agents of the anionic type include, for example, soaps; salts of aliphatic monoesters of sulphuric acid, for example sodium lauryl sulphate; salts of sulphonated aromatic compounds, for example sodium dodecylbenzenesulphonate; sodium, calcium or ammonium lignosulphonate; or butylnaphthalene sulphonate; and a mixture of the sodium salts of diisopropyl- and triisopropylnaphthalene sulphonates. Suitable agents of the non-ionic type include, for example, the condensation products of ethylene oxide with fatty alcohols such as oleyl alcohol or cetyl alcohol; or with alkyl phenols such as octyl phenol, nonyl phenol, and octyl cresol. Other non-ionic agents are the partial esters derived from long chain fatty acids and hexitol anhydrides, the condensation products of the said partial esters with ethylene oxide, and the lecithins.

These concentrates are often required to withstand storage for prolonged periods and after such storage, to be capable of dilution with water to form aqueous preparations which remain homogeneous for a sufficient time to enable them to be applied by conventional spray equipment. The concentrates may preferably contain 1-85% by weight of the active ingredient or ingredients. When diluted to form aqueous preparations such preparations may contain varying amounts of the active ingredient depending upon the purpose for which they are to be used.

The subject anthelmintic compounds may also be formulated as powders (dry seed treatment DS or water disperible powder WS) or liquids (flowable concentrate FS, liquid seed treatment LS), or microcapsule suspensions CS for use in seed treatments. The formulations can be applied to the seed by standard techniques and through conventional seed treaters. In use the compositions are applied to the nematodes, to the locus of the nematodes, to the habitat of the nematodes, or to growing plants liable to infestation by the nematodes, by any of the known means of applying pesticidal compositions, for example, by dusting, spraying, or incorporation of granules.

The compounds of the invention may be the sole active ingredient of the composition or they may be admixed with one or more additional active ingredients such

as nematicides, agents which modify the behavior of nematodes (such as hatching factors), insecticides, synergists, herbicides, fungicides or plant growth regulators where appropriate.

Suitable additional active ingredients for inclusion in admixture with the compounds of the invention may be compounds which will broaden the spectrum of activity of the compounds of the invention or increase their persistence in the location of the pest. They may synergise the activity of the compound of the invention or complement the activity for example by increasing the speed of effect or overcoming repellency. Additionally multi-component mixtures of this type may help to overcome or prevent the development of resistance to individual components.

The particular additional active ingredient included will depend upon the intended utility of the mixture and the type of complementary action required. Examples of suitable insecticides include the following:

a) Pyrethroids such as permethrin, esfenvalerate, deltamethrin, cyhalothrin in particular lambda-cyhalothrin, biphenthrin, fenpropathrin, cyfluthrin, tefluthrin, fish safe pyrethroids for example ethofenprox, natural pyrethrin, tetramethrin, s-bioallethrin, fenfluthrin, prallethrin, and 5-benzyl-3-furylmethyl-(E)-(1R,3S)-2,2-dimethyl-3-(2-oxothiolan-3-ylidenem ethyl) cyclopropane carboxylate;

b) Organophosphates such as profenofos, sulprofos, methyl parathion, azinphos-methyl, demeton-s-methyl, heptenophos, thiometon, fenamiphos, monocrotophos, profenophos, triazophos, methamidophos, dimethoate, phosphamidon, malathion, chloropyrifos, phosalone, terbufos, fensulphothion, fonofos, phorate, phoxim, pyrimiphos-methyl, pyrimiphos-ethyl, fenitrothion, or diazinon;

c) Carbamates (including aryl carbamates) such as pirimicarb, cloethocarb, carbofuran, furathiocarb, ethiofencarb, aldicarb, thiofurox, carbosulphan, bendiocarb, fenobucarb, propoxur, or oxamyl;

d) Benzoyl ureas such as triflumuron or chlorofluazuron;

e) Organic tin compounds such as cyhexatin, fenbutatin oxide, or azocyclotin;

f) Macrolides such as avermectins or milbemycins, for example such as abamectin, avermectin, and milbemycin;

g) Hormones and pheromones;

h) Organochlorine compounds such as benzene hexachloride, DDT, endosulphan, chlordane, or dieldrin;

i) Amidines, such as chlordimeform or amitraz;

j) Fumigant agents;

k) nitromethylenes such as imidacloprid.

In addition to the major chemical classes of insecticide listed above, other insecticides having particular targets may be employed in the mixture if appropriate for the intended utility of the mixture. For instance, selective insecticides for particular crops, for example stemborer specific insecticides for use in rice such as cartap or buprofezin, can be employed. Alternatively, insecticides specific for particular insect species/stages, for example, ovo-larvicides such as chlofentezine, flubenzimine, hexythiazox, and tetradifon; motilicides such as dicofol or propargite; acaricides such as bromopropylate or chlorobenzilate; or growth regulators such as hydramethylon, cyromazin, methoprene, chlorfluazuron, and diflubenzuron may also be included in the compositions.

Examples of suitable synergists for use in the compositions include piperonyl butoxide, sesamax, safroxan, and dodecyl imidazole.

Suitable herbicides, fungicides, and plant-growth regulators for inclusion in the compositions will depend upon the intended target and the effect required.

An example of a rice selective herbicides which can be included is propanil, an example of a plant growth regulator for use in cotton is "Pix", and examples of fungicides for use in rice include blasticides such as blasticidin-S. The ratio of the compound of the invention to the other active ingredient in the composition will depend upon a number of factors including type of target, effect required from the mixture, etc. However in general, the additional active ingredient of the composition will be applied at about the rate as it is usually employed, or at a slightly lower rate if synergism occurs.

The anthelmintic compounds according to the invention also show fungicidal activity and may be used to control one or more of a variety of plant pathogens. In a further aspect the invention therefore includes a method of combating fungi which comprises applying to a plant, to a seed of a plant, or to the locus of the plant or seed a fungicidally effective amount of a compound as herein defined or a composition containing the same. The invention further includes a fungicidal composition comprising

a fungicidally effective amount of a compound as herein defined and a fungicidally acceptable carrier or diluent therefor.

Examples of plant pathogens which the compounds or fungicidal compositions of the invention may control, methods by which fungi may be combatted and the form of suitable compositions, including acceptable carriers and diluents; adjuvants such as wetting, dispersing, emulsifying, and suspending agents; and other ingredients, such as fertilisers and other biologically active materials, are described, for instance, in International application No. WO 93/08180, the content of which is incorporated herein by reference.

All of the U.S. patents cited herein are hereby incorporated by reference.

Following are examples which illustrate procedures for practicing the invention. These examples should not be construed as limiting. All percentages are by weight and all solvent mixture proportions are by volume unless otherwise noted. For clarity the following abbreviations shall be used throughout the examples:

ACD:	Available Chemicals Directory
ACN:	Acetonitrile
AcOH:	Acetic Acid
AUC:	Area under curve
BAM:	Benzamidoxime
BOC:	t-Butoxycarbonyl
CI:	Chemical Ionization
CDI:	1,1'-Carbonyldiimidazole
1,2-DCE:	1,2-Dichloroethane
DCM:	Dichloromethane
DIOEA:	N,N-Diisopropylethylamine
DIC:	1,3 -Diisopropylcarbodiimide
DMAP:	4-(Dimethylamino)pyridine
EDC:	1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride
EI:	Electron Impact
ESI:	Electrospray ionization
HCI:	Hydrochloric Acid

HOBt: 1-Hydroxybenzotriazole

HPLC: High Performance Liquid Chromatography

LLE: Liquid Liquid Extraction

LC/MS: Liquid Chromatography/Mass Spectroscopy

O/N: Overnight

RT: Room Temperature

SLE: Solid-supported liquid-liquid extraction

THF: Tetrahydrofuran

TFA: Trifluoroacetic acid

QC: Quality Control

dH_2O Distilled Water

Example 1 – Preparation of Anthelmintic Compounds 1-46

The anthelmintic compounds of the subject invention can readily be produced using procedures well known to those skilled in the art.

A variety of anthelmintic compounds useful according to the subject invention can be readily prepared by a person skilled in this art having the benefit of the subject disclosure.

Example 2 – Nematicidal Activity of Anthelmintic Compositions 1-31

Caenorhabditis elegans adults were grown on Nematode Growth Medium (NGM) until they produced eggs, then the adults were removed.

The eggs were allowed to hatch, and the L1 larvae collected. See *The Nematode Caenorhabditis elegans* (1988) Cold Spring Harbor Laboratory Press. Using a Matrix Programmable Pipette, the L1s were distributed into 96-well tissue culture plates, 20 L1 in 50μl NGM per well. Antibiotic/Antimyotic was added to each well, and 1% by weight *E. coli* strain HB101. The subject anthelmintic compounds were stored at 5mM in 100% DMSO. 0.7μl of compounds 1-31 were added to the left-most column of wells to yield a final concentration of 70μM in 1.4% DMSO, with 1.4% DMSO only as the control. The compounds were then subjected to 5 more 3-fold dilutions from left to right to yield 6 column concentrations of 70μM, 23.3μM, 7.8μM, 2.6μM, 0.9μM, and 0.3μM. Plates were stored in air-tight Rubbermaid plastic boxes at 20°C. The nematodes had cleared

all control wells by day 4, and nematode viability was scored by visual examination under a 100x dissecting microscope on day 5. A visual viability scoring system was used as follows:

WORM VISUAL SCORING GUIDE

Lethality:

Dead	only stiff L1s (no movement)
Dead (L4)	worms are dead, but at a later larval stage
L1	majority of worms are L1 (based on size) worms move when plate is tapped
L2	majority of worms are L2 (based on size)
L3	majority of worms are L3 (based on size)
L4	majority of worms are L4 (based on size)

Partial Penetrance:

AD	majority of worms are adult
#AD	5 adult worms or less

Broodsize Reductions:

B!	sterile	(0 – 25 progeny)
B	low broodsize	(25 – 100 progeny)
~B	moderate broodsize	(100 – 250 progeny)
<	reduced broodsize	(250 – 500 progeny)
OK	no effect	(~ 1000+ progeny)

If several classes of worms exist in a well, then all classes are scored. If adults are present, then the brood score is also recorded. Thus, "L1/L2" would mean a mixture of L1's and L2's are present in the well. "L4/#AD/B" would mean that a mixture of L4's and adults are resent in the well. The "#AD" would mean that there are 6 or less adults, and the "B" would mean that there were 100 progeny or less.

The results are reported in Table 1. Column V1 has a compound concentration of 70μM with sequential 3-fold dilutions reported in columns V2, V3, V4, V5, and V6, respectively, such that the V6 concentration was 0.3μM.

TABLE 1

Dose Response Tracking					5 Day Visual Score					
DR#	IIIS Tracking Library #	Structure #	Source P	Well Address	V1	V2	V3	V4	V5	V6
1575	AKC 111	1	N2#93	5081:D10	Dead	Dead	L2	Dead(L3/L	#AD/B	OK
1647	AKC 112	2	N2#98	5090:A10	L2/L3	L2/L3	L2/L3	L3/L4	#AD/~B	OK
1466	AKC 113	3	N2#85	5061:A10	Dead	Dead	Dead	Dead(L2/L	L2/Dead(A	L4/#AD/B
1469	AKC 107	4	N2#86	5061:D10	Dead	Dead (L2/L3)	L2/L3	Dead(L4)	L4 Dead(A	L2/Dead(L
1477	AKC 114	5	N2#86	5061:D11	Dead	L3/Dead(L4)	L3	L3/Dead(L	L2/L3	~B
1476	AKC 108	6	N2#86	5061:C11	Dead	Dead	L1	L1	L1/L2	L1/L3
1473	AKC 115	7	N2#86	5061:1110	Dead	Dead(L2/L3)	L2/Dead(L2)	Dead(L2)	Dead(L2/L	L2/L3
035	AKC 119	11	N2#126	5393:B4	#AD/B	#AD/B	#AB/B	#AD/B	#AD/B	<
2059	AKC 110	12	N2#128	5399:C4	L1	L1	L1	L1	L1	L1
2083	AKC 120	13	N2#130	5449:C4	L1	L2/L3	L1	L1/L2	#AD/~B	OK
2032	AKC 121	14	N2#126	5389:C4	L1	L1	L1/L2	#AD/~B	#AD/B	<
2029	AKC 2153	15	N2#126	5379:C4	L1	L1	L1/L2	#AD/B	#AD/B	#AD/B
1962	AKC 122	16	N2#121	5373:B8	Dead	L1	#AD/B	#AD/B	#AD/B	OK
1388	AKC 104	17	N2#80	5022:C4	L1/1.2	L1/L2	L1/L2	#AD/B	L1/L2	L1/L2
1372	AKC 123	18	N2#79	5016:B8	L1	L1/L2	#AD/B	<	#AD/B	#AD/~B
1402	AKC 124	19	N2#81	5033:D8	#AD/B!	#AD/B!	L2/L3	L4/#AD/B	L4/#AD/B	L4/#AD/B
1396	AKC 125	20	N2#80	5031:G8	L2/Dead(L3)	L2/Dead(L4)	L2	L2	#AD/B	<

TABLE 1/Continued

Dose Response Tracking					5 Day Visual Score					
DR#	IIIS Tracking Library #	Structure #	Source P	Well Address	V1	V2	V3	V4	V5	
1393	AKC 105	21	N2#80	5031:G2	L2/Dead(L.3)	1.2/Dead(L3)	L2/Dead(L3)	L2/Dead(L	L2/Dead(L	L2/Dead(A
1164	AKC 126	22	N2#64	4724:E10	L1/L2	L1/L2	L1/L2	#AD/~B	~B	#AD/~B
1174	AKC 102	23	N2#65	4727:E8	L1/L2	L1/L2	L2/L3	L3	#AD/B	B
806	AKC 103	24	N2#149	4470:D10	L1/L2	Dead(L3/L.4)	Dead(L4)	B	L4/#AD/B	<
18	AKC 171	25	N2#2	2606:A1	Dead	L.2	Dead(L4)/#A	L2/L3	<	L2/L3
433	AKC 128	26	N2#31	3313:A10	Dead	Dead	Dead	L1	#AD/~B	OK
506	AKC 129	27	N2#37	3315:A10	Dead	Dead	L1/L2	L1/L2	OK	L1/L2
484	AKC 130	28	N2#35	3314:D10	Dead	#AD/~B	#AD/B	#AD/~B	OK	#AD/B!
486	AKC 131	29	N2#35	3314:F10	Dead	L1	#AD/~B	#AD/~B	#AD/~B	<
568	AKC 132	30	N2#41	3323:G4	Dead(1.2)	Dead	Dead	#AD/B	#AD/B	Dead
569	AKC 133	31	N2#41	3323:114	Dead	Dead	Dead	Dead	Dead	Dead
187	AKC 340	32	N2#14	2665:B5	L1	L1	#AD/B!	#AD/B!	#AD/B	B
133	AKC 134	33	N2#10	2640:A11	Dead	Dead	Dead	#AD/B	#AD/B	OK
149	AKC 135	34	N2#11	2641:A8	Dead	L1	L1/L2	#AD/B	~B	#AD/B!

Example 3 – Nematicidal Activity of Anthelmintic Compositions 32-46

The *C. elegans* nematode activity assay for anthelmintic compounds 32-46 was similar to that described in Example 2 above, except for the following noted differences. The compound concentrations were adjusted to 140 μM and subjected to 2-fold dilutions to yield 140μM, 70μM, 35μM, 17.5μM, 8.8μM, 4.4μM, 2.2μM, and 1.09μM. The visual evaluation of viability was conducted at Day 4, and the results are presented in Table 2.

Table 2.

Compound	μM Concentration							
	140	70	35	17.5	8.8	4.4	2.2	1.09
AKC-138	L1	L1	L1	L2	~B	OK	OK	OK
AKC-144	L3/L4	L4/AD/B	B	~B	OK	OK	OK	OK
AKC-141	L1	L1	L1	<	OK	OK	OK	OK
AKC-116	L1/L2	L2/L3	L3	B!	B	OK	OK	OK
AKC-117	L1/L2	L2/L3	L3	B!	B	<	OK	OK
AKC-118	L2	L2/L3	L3	L4/AD/B!	B	~B	OK	OK
Control	OK	OK	OK	OK	OK	OK	OK	OK

Example 4 - Activity Against Nematode (*C. elegans*) Eggs

Compositions of the subject invention are surprisingly found to be ovicidal. The following procedures are used to test for lethal effects against nematode eggs.

Materials

As referred to herein, "S Medium" refers to "S basal" supplemented with $CaCl_2$, $MgSO_4$, and a trace metals solution as follow:

S basal

NaCl	5.857 g
1M potassium phosphate (pH 6)	50.0 ml

Cholesterol (5mg/ml in EtOH)	1.0 ml
dH_2O	
	1 L

The above preparation is then autoclaved. S basal can be stored until needed.

Just prior to use, S Medium is made from S basal by adding, asceptically, the following components to 1L S basal (components should first be autoclaved separately):

1M potassium citrate (pH 6)	10 ml
Trace metals solution (see below)	10 ml
1M $CaCl_2$	3 ml
1M $MgSO_4$	3 ml

Trace Metals solution

Na_2EDTA	1.86 g	(to 5mM)
$Fe_2SO_4 \cdot 7H_20$	0.69 g	(to 2.5mM)
$MnCl_2 \cdot 4H_2O$	0.20 g	(to 1mM)
$ZnSO_4 \cdot 7H_20$	0.29 g	(to 1mM)
$CuSO_4 \cdot 5H_20$	0.025 g	(to 0.1mM)
dH_20		
		1 L

Procedure:

1. Make anthelmintic compound dilutions as indicated in Examples 2-3.
2. To 500 µl of each dilution, added 10 µl of eggs (estimated >200 eggs/10 µl).
3. Mixed well and allowed to incubate at room temperature for from 30 minutes to 3 hours.
4. Centrifuge at 2000 rpm for 5 minutes at room temperature.
5. Pipette off supernatant.
6. Re-suspend in 500 µl S Medium.
7. Centrifuge at 2000 rpm for 5 minutes at room temperature

8. Pipette off supernatant.
9. Re-suspend in 300 µl S Medium.
10. Transfer 300 µl into 24-well tissue culture bioassay tray.
11. Add 2 µl of stationary phase *E. coli* to each well.
12. Score after 3 days at room temperature in the dark.

Example 5 – Additional Observations of Activity Against Nematode (*C. elegans*) Eggs

Additional tests are conducted to confirm the ovicidal activity. The following procedures are used.

1. Make anthelmintic compound dilutions to 2X concentrations shown in Example 4.
2. Distribute 0.5 ml of each dilution into 1.5-ml Eppendorf tubes.
3. Add 0.5 ml of *C. elegans* egg preparation to 0.5 ml 2X dilution to yield final exposure concentration.
4. Mix well and allow to incubate at room temperature for from 30 minutes to 3 hours.
5. Centrifuge at 2000 rpm for 5 minutes at room temperature.
6. Pipette off supernatant and re-suspend in 1.5 ml S Medium.
7. Spin as above for 2 minutes.
8. Pipette off supernatant and re-suspend in 1.5 ml S Medium.
9. Repeat #7.
10. Pipette off supernatant and re-suspend in 1.0 ml S Medium.
11. Add 280 µl of S Medium to each well of 24-well tissue culture plate.
12. Add 20 µl of each treated (and control) sample in triplicate into the respective wells.
13. Score after 3 days at room temperature in the dark.

Example 6 – Preparation of Anthelmintic Compounds 47, as specifically exemplified by Compounds 48 -226

While the anthelmintic compounds of the subject invention can readily be produced using procedures well known to those skilled in the art, the following is a preferred method of producing anthelmintic Compounds 47, and exemplified Compounds

48-226, as shown in Figures 47, 48-226. The general library scheme resulting in Compounds 47 is depicted in Figure 227.

The experiments to optimize the reaction conditions as well as to synthesize the standards were generally performed in 12 x 75 mm test tubes using a preheated VWR Brand Dry Block Heater (VWR Scientific, catalog #13259-030) with a 16-hole, 12-13 mm test tube heating block (VWR Scientific, catalog #13259-120). Later experiments and precursor validation were performed in Beckman 2 mL square-well microtiter plates. Most reagent additions during the validation phase of development were accomplished with either single-channel pipettors (e.g. Oxford Benchmate or Eppendorf repeator pipets) or 8-channel Matrix pipettors. All the acid chloride and sulfonyl chloride precursors are commercially available and were used as received. EDC was purchased from Advanced ChemTech. DMAP was purchased from Aldrich. DIPEA and Et3N were from Acros. Dowex-1 anion exchange resin (hydroxide form, Sigma catalog number I-9880) was washed according to the following sequence: methanol, chloroform, 50% aqueous methanol, using one portion per solvent. SLE's were performed using bulk packing material ("hydromatrix") supplied by Varian (catalog number 0019-8003) and used as received. Some starting materials were synthesized and their preparation is described below.

Preparation of Starting Materials.

The ten amidoximes employed to make the subject compounds are either commercially available or can be prepared by treatment of the corresponding commercially available benzonitriles (see Table 8 and Table 11) with hydroxylamine hydrochloride and base in ethanol in moderate to high yields. Six of the sixteen BOC-amino acids employed in the manufacturing process (see Table 9) were purchased from various vendors. The remaining 10 were prepared in high yield by treatment of the corresponding commercially available amino acids with di-t-butyl dicarbonate and NaOH in aqueous THF. All the synthesized precursors were characterized by HPLC, MS, and NMR. In cases where BOC-amino acids could not be satisfactorily characterized by these methods, these intermediates were subsequently characterized by conversion to the corresponding 1,2,4-oxadiazole.

Method A:

4-Methoxybenzamidoxime. To a stirred solution of 12.0 g (0.172 mol) of hydroxylamine hydrochloride and 22.2 g (0.172 mol) of DIPEA in 350 mL of ethanol was added 19.2 g (0.144 mol) of 4-methoxybenzonitrile. The resulting mixture was stirred at room temperature for 18 h overnight, then concentrated in vacuo. The oily residue was triturated with 300 mL of water and the resulting precipitate was filtered, washed with H2O, then dried in vacuo to afford 17.5 g (73%) of the desired product. MS (ESI) m/z 167 (M+H, 100%). ^{1}H-NMR (DMSO-d_6) δ 3.75 (s, 3H), 5.75 (s, 2H), 6.90 (d, 2H), 7.65 (d, 2H), 9.45 (s, 1H).

Method B:

2-Methoxybenzamidoxime. A suspension of 11.5 g (0.165 mol) of hydroxylamine hydrochloride, 17.5 g (0.165 mol) of Na_2CO_3, and 20.0 g of 2-methoxybenzonitrile in 350 mL of EtOH and 30 mL of H_2O was heated at -80° C for 10 h. After cooling to room temperature, the mixture was filtered, and the filter-cake washed with EtOH. The filtrate was concentrated in vacuo to give a semi-solid product which was triturated with a mixture of ether/hexane, and the white solid was filtered, washed with hexane then dried to afford 17.4 g (70%) of the desired product. MS (ESI) m/z 167 (M+H, 100%). ^{1}H-NMR (300 MHz, DMSO-d_6) δ 3.81 (s, 3H), 5.6 (s, 2H), 6.90 (t, 1H), 7.10 (d, 1H), 7.35 (t, 2H), 9.40 (s, 1H).

4-Methylbenzamidoxime (Method A). A mixture of 19.5 g (0.167 mol) of 4-methylbenzonitrile, 13.9 g (0.20 mol) of hydroxylamine hydrochloride, and 25.8 g (0.20 mol) of DIPEA in 350 mL of EtOH afforded 21.6 g (86%) of a white solid. MS (ESI) m/z 150 (100%). ^{1}H-NMR (DMSO-d_6) δ 2.28 (s, 3H), 5.77 (s, 2H), 7.2 (d, 2H), 7.6 (d, 2H), 9.57 (s, 1H).

Piperonylamidoxime (Method A). A mixture of 20.0 g (0.136 mol) of piperonylonitrile, 11.3 g (0.163 mol) of hydroxylamine hydrochloride, and 21.0 g (0.163 mol) of DIPEA in 350 mL of EtOH gave 16.4 g (67%) of light yellow crystals. MS (ESI) m/z 180 (100%). ^{1}H-NMR (DMSO-d_6) δ 5.75 (s, 2H), 6.03 (s, 2H), 6.88 (d, 1H), 7.23 (d, 2H), 9.51 (s, 1H).

3,4-Dimethylbenzamidoxime (Method A). A mixture of 20.0 g (0.152 mol) of 3,4-dimethylbenzonitrile, 12.7 g (0.183 mol) of hydroxylamine hydrochloride, and 23.6 g (0.183 mol) of DIPEA in 350 mL of EtOH to afford 17.0 g (68%) of light yellow crystals after recrystallization from ethyl acetate. MS (ESI) m/z 165 (M+H, 100%). ^{1}H-NMR (DMSO-d_6) δ 2.23 (s, 6H), 5.75 (s, 2H), 7.2 (d, 1H), 7.36-7.48 (m, 2H), 9.5 (s, 1H).

4-Methylsulfonylbenzamidoxime (Method A). A solution of 22.5 g (0.124 mol) of 4-methylsulfonylbenzonitrile, 10.4 g (0.149 mol) of hydroxylamine hydrochloride, and 19.3 g (0.149 mol) of DIPEA in 350 mL of EtOH afforded 25.3 g (95%) of a white solid. MS (ESI) m/z 215 (M+H, 100%). ^{1}H-NMR (DMSO-d^6) δ 3.23 (s, 3H), 6.0 (s, 2H), 7.87 (s, 4H), 9.98 (s, 1H).

3-Methoxybenzamidoxime (Method A). The mixture from 20.0 g (0.150 mol) of 3-methoxybenzonitrile, 12.5 g (0.180 mol) of hydroxylamine hydrochloride, and 23.2 g (0.180 mol) of DIPEA in 350 mL of EtOH was concentrated in vacuo and the residue was filtered through a short plug of silica gel (eluant: ethyl acetate). The filtrate was concentrated in vacuo and triturated with water. The resulting solid was filtered and dried to afford 19.5 g (78%) of the desired product. MS (ESI) m/z 167 (M+H, 100%). ^{1}H-NMR (DMSO-d_6) δ 3.77 (s, 3H), 5.85 (s, 2H), 6.9-7.35 (m, 4H), 9.7 (s, 1H).

3-Methylbenzamidoxime (Method A). The mixture from 20.0 g (0.171 mol) of 3-methylbenzonitrile, 14.2 g (0.205 mol) of hydroxylamine hydrochloride, and 26.4 g (0.205 mol) of DIPEA in 350 mL of EtOH was concentrated in vacuo and the residue was partitioned between DCM and a minimum amount of water. The layers were separated and the DCM layer was stirred with a few grams of silica gel for 10 min. The suspension was filtered then concentrated in vacuo to afford 21.3 g (83%) of the desired product as a solid. MS (ESI) m/z 151 (M+H, 100%). ^{1}H-NMR (DMSO-d_6) δ 2.33 (s, 3H), 5.75 (s, 2H), 7.2-7.5 (m, 4H), 9.6 (s, 1H).

4-n-Butoxybenzamidoxime (Method A). The residue from a mixture of 20.0 g (0.114 mol) of 4-n-butoxybenzonitrile, 9.52 g (0.137 mol) of hydroxylamine

hydrochloride, and 17.7 g (0.137 mol) of DIPEA in 350 mL of EtOH was triturated with water. The resulting solid was suspended in hexane, stirred for 1 h at room temperature, and filtered to afford 21.8 g (92%) of a white solid. MS (ESI) m/z 209 (M+H, 100%). ^{1}H-NMR (DMSO-d_6) δ 0.85 (s, 3H), 1.35-1.74 (m, 4H), 3.95 (m, 2H), 5.8 (s, 2H), 6.90 (d, 2H), 7.64 (d, 2H), 9.50 (s, 1H).

General Procedure for BOC-protection:

4-(BOC-aminomethyl)benzoic acid. To a solution of 5.80 g (0.145 mol) of NaOH in 250 mL of H_2O was added 20.0 g (0.132 mol) of 4-(aminomethyl)benzoic acid. After the acid had completely dissolved, a solution of 31.8 g (0.145 mol) of di-t-butyl-dicarbonate in 100 mL of THF was added. The mixture was stirred at room temperature overnight then concentrated in vacuo to remove most of the THF. The resulting aqueous layer was acidified to pH 2-3 with solid $KHSO_4$. The mixture was extracted with ether and the combined extracts dried ($MgSO_4$) and concentrated in vacuo to afford 32.7 g (99%) of a white solid. ^{1}H-NMR (300 MHz, DMSO-d_6) δ 1.39 (s, 9H), 4.20 (d, 2H), 7.36 (d, 2H), 7.48 (t, 1H), 7.88 (d, 2H).

BOC-trans-4-(Aminomethyl)cyclohexanecarboxylic acid. According to the general procedure, a mixture of 15.7 g (0.10 mol) trans-4-(aminomethyl)cyclohexanecarboxylic acid, 4.40 g (0.110 mol) of NaOH, and 24.0 g (0.110 mol) of di-t-butyl-dicarbonate in 100 mL of THF and 250 mL of water gave 23.2 g (90%) of the desired product as a white solid. ^{1}H-NMR (300 MHz, DMSO-d_6) δ 0.75-0.95 (m, 2H), 1.35 (s, 9H), 1.22-1.3 (m, 3H), 1.73 (d, 2H), 1.85 (d, 2H), 2.13 (m, 1H), 2.80 (t, 2H), 6.79 (t, 1H).

BOC-DL-3-Aminocyclohexanecarboxylic acid. According to the general procedure, a mixture of 20.0 g (0.14 mol) of the 3-aminocyclohexanecarboxylic acid (stereochemistry undefined), 6.16 g (0.154 mol) of NaOH, 33.49 g (0.154 mol) of $(BOC)_2O$ in 120 mL THF and 250 mL water afforded 28.7 g (84.4%) of a white solid.

BOC-4-Aminocyclohexanecarboxylic acid. According to the general procedure, a mixture of 20.0 g (0.140 mol) of the 4-aminocyclohexanecarboxylic acid (a cis/trans mixture), 6.16 g (0.154 mol) of NaOH, and 33.5 g (0.154 mol) of $(BOC)_2O$ in 120 mL

THF and 250 mL water afforded 24.2 g (71%) of the desired product as a colorless solid.

BOC-DL-3-Aminobutyric acid. To a solution of 6.40 g (0.160 mol) of NaOH in 250 mL of water was added 15.0 g (0.145 mol) of DL-3-aminobutyric acid. To this solution was added 160 mL (0.160 mol) of 1.0 M solution of $(BOC)_2O$ in THF. The resulting mixture was stirred at room temperature overnight, then processed according to the general procedure to afford 22.5 g (76%) of the desired product as a white solid.

BOC-DL-β-Aminoisobutyric acid. According to the general procedure, a mixture of 20.0 g (0.194 mol) of DL-β-aminobutyric acid, 8.52 g (0.213 mol) of NaOH, 213 mL (0.213 mol) of 1.0 M $(BOC)_2$ O in THF and 250 mL water gave 38.6 g (98%) of a white solid. ^{1}H-NMR (300 MHz, DMSO-d6) δ 0.17 (d, 3H), 0.54 (s, 9H), 1.60-1.70 (m, 1H), 2.02-2.12 (m, 1H), 2.25-2.35 (m, 1H), 6.00 (t, 1H), 11.35 (s,1H)

BOC-DL-3-Amino-3-phenylpropionic acid. According to the general procedure, a mixture of 20.0 g (0.121 mol) of DL-3-amino-3-phenylpropionic acid, 5.32 g (0.133 mol) of NaOH, 133 mL (0.133 mol) of 1.0 M $(BOC)_2O$ in THF and 250 mL of water gave 25.7 g (80%) of a white solid. ^{1}H-NMR (300 MHz, DMSO-d_6) δ 0.50 (s, 9H), 1.71-1.80 (m, 2H), 4.05 (t, 1H), 6.35-6.45 (m, 5H), 6.70 (d, 1H), 11.37 (s, 1H).

BOC-DL-Nipecotic acid. To a stirred solution of 4.19 g (0.105 mol) of NaOH in 100 mL of water was added 13.0 g (0.101 mol) of DL-nipecotic acid. This solution was cooled in ice water bath then treated with 100 mL (0.100 mol) of 1.0 M (BOC)2O in THF. The resulting mixture was stirred at room temperature for 15 h, then concentrated in vacuo to remove most of the THF. The resulting aqueous solution was washed with ether, then acidified with H_3PO_4 (10 mL). The white precipitate was filtered, washed with water, and dried under high vacuum to afford 21.5 g (93%) of a white powder. ^{1}H-NMR (300 MHz, DMSO-d6) δ 1.38 (s, 9H), 1.42-1.63 (m, 2H), 1.86-1.91 (m, 2H), 2.24-2.32 (m, 1H), 2.81 (dt, 1H), 3.66 (br d, 1H), 3.89 (br s, 2H), 12.3 (s, 1H).

BOC-4-Piperidinoacetic acid. A suspension of 24.3 g (0.140 mol) of 4-pyridylacetic acid hydrochloride and 2.07 g of PtO_2 in 150 mL AcOH was hydrogenated at 50 psi. After hydrogen uptake has ceased, the mixture was kept at 50 psi for 30 min, then it was purged with nitrogen for 15 min. The mixture was filtered and the catalyst was washed with water. CAUTION: THE CATALYST MUST BE KEPT WET WITH

WATER AT ALL TIMES, OTHERWISE A FIRE WILL RESULT. DO NOT WASH THE CATALYST WITH FLAMMABLE ORGANIC SOLVENTS SUCH AS METHANOL OR ETHANOL. The filtrate and washings were concentrated in vacuo to give a colorless semisolid mixture which was triturated with 250 mL of diethyl ether and the resulting suspension was stirred for few hours. The solid was filtered, washed with ether and hexane, then dried in vacuo to give 25.4 g (100%) of 4-piperidineacetic acid hydrochloride as a white powder.

To a solution of 12.0 g (0.300 mol) of NaOH in 300 mL water was added the solid isolated above. The resulting solution was cooled in an ice water bath and treated with 100 mL of THF, followed by 140 mL (0.140 mol) of 1.0 M $(BOC)_2O$ in THF. The resulting solution was stirred at room temperature overnight. The THF was removed in vacuo and the resulting aqueous solution was washed with ether, then acidified to pH 1-2 with 85% H3PO4. The solution was extracted with ethyl acetate, then the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo to give 29.1 g (86%) of a colorless, viscous oil which solidified upon drying in vacuo to give a white solid. ^{1}H-NMR (300 MHz, DMSO-d_6) δ 1.01 (dq, 2H), 1.37 (s, 9H), 1.60 (br d, 2H), 1.73-1.82 (m, 1H), 2.12 (d, 2H), 2.67 (br s, 2H), 3.88 (br d, 2H), 12.1 (s, 1H).

BOC-DL-3-(3-piperidino)propionic acid. A suspension of 24.8 g (0.166 mol) of 3-(3-pyridyl)acrylic acid in DCM was treated with 45 mL of 4N HCl in dioxane for 2h, then diluted with ether and filtered. The solid was washed with ether, and dried in vacuo to afford 31.0 g of a colorless solid. The solid was suspended in 150 mL of acetic acid and 2.71 g of PtO2 was added. The suspension was hydrogenated at 50-55 psi until hydrogen uptake has ceased. The mixture was diluted with 50 mL of water, filtered, and the catalyst washed with water, keeping the catalyst wet at all times. The combined filtrate and washings were concentrated in vacuo to give 31.0 g (96%) of the piperidinopropionic acid as a white powder.

The above solid was added to a stirred solution of 13.1 g (328 mmol) of sodium hydroxide in 250 mL of water, then the reaction mixture cooled in an ice water bath. After the solids had dissolved, 160 mL (160 mmol) of a 1.0 M solution of $(BOC)_2O$ in THF was added via an addition funnel. An additional 80 mL of THF was used to wash the addition funnel. The reaction mixture was stirred for 68 hours, allowing the ice bath to warm up to room temperature. The mixture was concentrated in vacuo to remove

most of the THF and the resulting aqueous solution washed with diethyl ether (300 mL). The aqueous phase was acidified to pH 2-3 with 15 mL of 85% phosphoric acid, the solution was then extracted with ethyl acetate (300 mL). The extract was washed with saturated aqueous NaCl (2x100 mL), dried (Na_2SO_4) and concentrated in vacuo to afford 39.5 g (96%) of a white solid. ^{1}H-NMR (300 MHz, DMSO-d_6) δ 1.00-1.44 (m, with s at 1.37 ppm, 13H), 1.52-1.57 (m, 1H), 1.70-1.75 (m, 1H), 2.23 (t, 2H), 2.78 (br t, 2H), 3.68 (br s, 2H), 12.1 (s, 1H).

Library Synthesis.

Step A: O-Acylation and Cyclization.

Caution: Moisture Sensitive Reactions. The following chemistry is moisture-sensitive. All solutions must be prepared from anhydrous solvents (e.g. Aldrich "Sure/Seal"), ideally just before they are to be added to the plates. Furthermore, reagent additions should be done as quickly as possible to minimize moisture accumulation from the atmosphere on standing.

To 2-mL square well Beckman plates was added 700 (L (0.140 mmol) of a 0.2 M solution of the BOC-amino acids in 1,4-dioxane using a Robbins HydraTM 96-well dispenser (Robbins Scientific, catalog number 1029-80-1) to the assigned wells. Each BOC-amino acid solution was then treated with, in the following sequence, 80 (L (0.04 mmol) of a 0.5 M solution of 4-DMAP in 1,4-dioxane and 140 (L (0.140 mmol) of a 1.0 M solution of EDC in CHCl3, using the Robbins HydraTM to add both reagents. The resulting mixtures were shaken on an IKL orbital shaker (VWR Scientific, catalog number 33994-220) for 5-10 min followed by 700 (L (0.140 mmol) of a 0.2 M solution of the appropriate hydroxyamidine in 1,4-dioxane. Each plate was covered with a teflon sheet, clamped and shaken on a Lab line reciprocal shaker (VWR Scientific, catalog number 57008-195; setting 6) for a minimum of 18 hours.

The plates were removed from the shaker and unclamped. To each well was added 20 (L (0.140 mmol) of neat Et3N. The plates were then shaken, unclamped, on a reciprocal shaker (setting 5) for 4-5 minutes, then the plates were heated, uncovered, in a preheated (100^0-105^{0}C) nitrogen-purged oven (VWR Scientific, catalog number 52201-656) for 7 hours. The plates were removed from the oven and allowed to cool to

room temperature. Generally the solvents will have evaporated when the plates are removed from the oven.

The contents of each well was dissolved in 1.0 mL of $CHCl_3$ then 300 μL of 10% aqueous citric acid solution was added to each well. The plates were shaken on a reciprocal shaker for 2 h. The two-phase mixtures were transferred to Polyfiltronics plates (type PP, 10 (m) with wells previously half-filled with hydromatrix material and pre-activated with 500 (L of 10% aq. citric acid and the plates were placed over 2-mL square-well Beckman plates. Each source well was rinsed once with 250 (L of $CHCl_3$ then transferred to the Polyfiltronics plate. Another 2x250 (L of CHCl3 were added to each well of the Polyfiltronics plate. After the contents of the wells were allowed to drain, the collection plates were concentrated in a Genevac evaporator for 3-4 h (Atlas, catalog number HT-12-CDOP).

Step B: BOC removal.

Each well was treated with 1.0 mL of a 1:1 mixture (v:v) of TFA in DCM. A teflon sheet was placed on top of each plate secured with a rubber band and was shaken on a reciprocal shaker for 2 hours. The plates were concentrated in the Genevac evaporator for 3-4 h using the ramping function. After evaporation, the resulting well contents of the plates were redissolved in 1.0 mL of 50% aqueous ACN, and the plates were shaken on an IKL Works microtiter plate shaker (VWR Scientific, catalog number 33994-220) for 30 min or the well contents were agitated in parallel using a modified Chiron Mimetopes "PIN" holder with fitted with 96 pegs to dissolve the samples before being frozen in a -80°C freezer (Revco, catalog ULT-2586-7 A) for at least 5 h (preferably overnight). The plates were then lyophilized in a tray lyophilizer (Virtis Unitop, catalog number 800L; tray temperature: 20 ^{0}C) for 18 h.

Step C: Acylation.

Using the Robbins HydraTM, the lyophilized products were treated with 500 μL (0.322 mmol) per well of a 0.65 M solution of DIPEA in $CHCl_3$ and shaken for 5-10 min. To each mixture was added 840 μL (0.126 mmol) of the appropriate acylating reagent (see Table 10) as a 0.15 M solution in $CHCl_3$, employing the Robbins HydraTM for the

reagent additions. Each plate was covered with a teflon sheet, clamped, and shaken on a reciprocal shaker for 18 h.

The plates were removed from the shaker and 300 μL of a 10% aqueous Na_2CO_3 solution was added to each well, using the Robbins HydraTM. The plates were shaken on a reciprocal shaker for 2 h, then the mixtures were transferred using the Robbins HydraTM to Polyfiltronics plates (PP, 10 μm) with wells previously half-filled with hydromatrix material and pre-activated with 500 μL of 10% aqueous Na_2CO_3. The plates were placed over 2-mL square-well Beckman plates. Each well was rinsed once with 250 μL of $CHCl_3$ which was collected in the Beckman plates. Another 2x250 μL of $CHCl_3$ was added to each well of the Polyfiltronics plates and allowed to drain into the Beckman plates. The Beckman plates should be about 3/4 full (ca. 1.5 mL) with solvent.

To each well was added 300 μL of 2 N aqueous HCl and the plates were shaken on a reciprocal shaker for 2 h. The mixtures were transferred to Polyfiltronics plates (PP, 10 (m) with wells previously half-filled with hydromatrix material and pre-activated with 500 μL of 2 N HCl per well. The plates were placed over a 2-mL square-well Beckman plates with wells previously loaded with 100-120 mg of Dowex-1 anion exchange resin. Each source well was rinsed with 2x250 μL of $CHCl_3$ then transferred to the Polyfiltronics plates. Another 250 μL of $CHCl_3$ were added to each well of the Polyfiltronics plates. After the plates were allowed to drain, the Beckman collection plates were put into a plastic container which was tightly-capped and shaken on a reciprocal shaker overnight.

The mixtures were transferred, using the Robbins HydraTM fitted with small gauge needles to prevent clogging by the resin, to Polyfiltronics plates (PP, 10 μm) with wells previously loaded with a thin layer of silica gel (ca 30-40 mg; Baxter Scientific Products, 60┼, 230-400 mesh; catalog number C4582-85). The Polyfiltronics plates were placed on top of 2-mL Beckman plates. Each well of the reaction plates were rinsed with $CHCl_3$ (2x250 μL) and transferred to the Polyfiltronics plates. The solvent was evaporated on the Genevac evaporator for 3-4 hours.

ACN (1.25 mL/well) was added and the plates were shaken on an orbital shaker for 30 min then sonicated for another 15-20 min. The plates were centrifuged for 30 min in either the Savant or Genevac evaporators without applying heat or vacuum. The resulting solutions were transferred by the Robbins HydraTM to a set of second, TARED

2-mL square-well Beckman plates. The plates were placed in the -80°C freezer for at least 5 h (preferably overnight), then lyophilized in the tray lyophilizer (tray temperature: 20 ^{0}C) for 18 h overnight.

Note on Solvents for QC. Samples submitted for direct injection QC analysis must be diluted with a mixture of 90% ACN and 10% of a 2.0 molar solution of ammonia in methanol (Aldrich; catalog number 34,142-8). The use of ammonia in methanol as a buffer for QC analysis improved ionization during direct injection analysis of samples for this library.

Development.

Early development experiments were run in 12x75 mm test tubes and reactions were heated in a VWR Scientific Dry Block heater. All SLE and other purification experiments were done in Polyfiltronics plates.

(A). Hydroxyamidine Synthesis. In most cases these precursors were prepared using literature methods. Since only one hydroxamidine (ACD #31485) was commercially available, the remaining 9 were synthesized as shown in Figure 228 from a benzonitrile (1) and hydroxylamine hydrochloride. Heating was sometimes necessary to drive the reaction to completion.

Other conditions explored for hydroxyamidine preparation included several bases (K_2CO_3, Na_2CO_3, $NaOCH_3$, Et_3N and DIPEA), and solvents (methanol or ethanol). The most suitable conditions identified were NH_2OH•HCl/DIPEA/ethanol at room temperature as described above or NH_2OH•HCl/Na_2CO_3/aqueous ethanol at 80 ^{0}C.

(B). BOC-amino Acids. While most commercially available BOC-α-amino acids failed to give product with sulfonyl chlorides, the use of acid chlorides did afford the desired products. Additional BOC-amino acids needed to expand the diversity for the library were synthesized from commercially available amino acids with the exception of two cases which were prepared by catalytic hydrogenation of a pyridine-containing acid and subsequent BOC-protection. An example is shown in Figure 229.

Acid Coupling and Cyclization (STEP A). There was ample literature precedent for the coupling of the hydroxyamidines to the BOC-amino acid and subsequent cyclization to afford the 1,2,4-oxadiazole ring. For development of a suitable production method for parallel synthesis in microtiter plates, various coupling agents were used

including CDI, DIC and EDC, with the latter being preferred since most of the byproducts derived from it could be removed by SLE. Bases such as DBU and triethylamine were explored in addition to catalysts such as 4-DMAP and HOBt. Lastly, several solvents and solvent mixtures were also investigated, including toluene, 1,4-dioxane, p-xylene, 1,2-dichloroethane, THF/1,4-dioxane, DCM/1,4-dioxane, and $CHCl_3$/1,4-dioxane. Ultimately EDC and 4-DMAP in a mixture of $CHCl_3$ and 1,4-dioxane were established as the best conditions for O-acylation. Cyclization of the O-acylated hydroxyamidines was done in situ in this solvent mixture by heating for a minimum of seven hours. Incomplete cyclization was noted with shorter heating times; however prolonged heating (>24 hours) resulted in the formation of additional byproducts that were not identified.

Purification at this stage was accomplished with 10% aqueous citric acid using standard SLE material. The extraction solvent employed was $CHCl_3$. Other solvents for the SLE step were not investigated.

BOC Removal and Acylation (STEP B). Use of both TFA in DCM or 4 N HCl in 1,4-dioxane cleanly gave the desired salts of the amines. While the latter conditions were expected to be easier to use in production since the solvent could be removed by lyophilization, this turned out to be more difficult in practice, primarily due to solubility problems of the resulting HCl salts. The use of TFA/DCM for the deprotection step, while avoiding the salt solubility issue described above, had other problems. Removal of the residual TFA by simple evaporation on the Genevac or Savant gave erratic results due to the presence of excess TFA which was not being completely neutralized when the base and acylator were added. Lyophilization of the evaporated plates from aqueous ACN circumvented this problem. The TFA salts were generally more soluble in $CHCl_3$ used in the acylation step.

STEP C was optimized for solvent and base. Solvents explored included 1,2-DCE, DCM, ethyl acetate, THF, and $CHCl_3$; bases included DIPEA and NMM. The best combination was DIPEA in $CHCl_3$. Purification of the final products was accomplished first with a basic SLE with 1 N aqueous KOH or 10% aqueous Na_2CO_3. The latter was preferred due to possible destruction of the SLE material with KOH. This purification step was followed by an acidic SLE with 2 N HCl. Both acidic (Amberlite IR-120) and basic (Amberlite IRA-67) ion exchange resins were evaluated as alternatives to the SLE steps but results were inconsistent. Due to the number of SLE steps required

for the library, the scale of the library was established at 140 μmol per well to compensate for losses in the purification steps.

Filtration of the final products through a thin layer of silica gel reduced the amounts of unacylated amines to less than 8% as determined by HPLC-UV at 214 nm by AUC. In addition, this step eliminated many strongly-charging minor byproducts as seen by LC-MS.

Example 7: Nematicidal Activity of Anthelmintic Compositions 48-226

The nematicidal activity of anthelmintic Compositions 48-226 were determined in accordance with the procedure outlined in Example 2. The results are reported in Table 3.

Table 3

			HTS Data												
HTS Tracking			Initial HTS Run			Follow-up HTS Run				5 Day Visual Score					
AKC #	MP #	Well	mOD	% Run Standard	Visual Score	mOD	% Run Standard	Visual Score	Well Address	V1	V2	V3	V4	V5	V6
810	4440	E6	157	115%	L4/AD/B! - Few Eggs	145	123%	L4/AD/B! - No P	4440:E6	B	<	OK	OK	OK	OK
811	4440	D9	146	107%	L4/AD/B	150	127%	L1/L2	4440:D9	L1/L2/L4	<	OK	OK	OK	OK
812	4441	F6	149	110%	L4/AD/B	149	126%	B! - Few Eggs	4441:F6	~B	OK	OK	OK	OK	OK
813	4442	B3	150	110%	5AD/B	133	113%	B	4442:B3	L1	OK	OK	OK	OK	OK
814	4442	B7	146	107%	Dead	152	129%	L1/L2	4442:B7	Dead	#AD/B	OK	OK	OK	OK
815	4442	B10	149	110%	4AD/B!	154	131%	Dead	4442:B10	Dead	L1/L2/L3	OK	OK	OK	OK
816	4442	C10	147	108%	2AD/B	144	122%	Dead (L2/L3)	4442:C10	Dead(L4)	#AD/B	OK	OK	OK	OK
										L1	L1	L1	L1	OK	OK
817	4442	D10	142	104%	L4/AD/B!	129	109%	B	4442:D10	L1/L2/L4	<	OK	OK	OK	OK
818	4442	A11	129	95%	L2/L3	127	108%	L2	4442:A11	L1/L2/L3	L2/L3	~B	<	OK	OK
819	4442	D11	146	107%	L2/L3	138	117%	L3	4442:D11	L1/L2	<	OK	OK	OK	OK
820	4443	C5	120	88%	B - Unhatched Eggs	96	81%	B - Lots Unhatched Eggs	4443:C5	OK	OK	OK	OK	OK	OK
821	4443	C6	126	93%	B - Unhatched Eggs	111	94%	B! - Healthy, Unhatched Eggs	4443:C6	<	OK	OK	OK	OK	OK
822	4443	D6	149	110%	L4	131	111%	B! - Unhatched Eggs, Few Eggs	4443:D6	~B	OK	OK	OK	OK	OK
823	4444	D3	144	106%	L4/AD/B	143	121%	B	4444:D3	<	OK	OK	OK	OK	OK
										B!	B!	B!	OK	OK	OK
824	4444	D8	160	118%	L2/L3/1AD/B!	153	130%	L2/L3	4444:D8	#AD/B	<	OK	OK	OK	OK
825	4445	D3	157	115%	L3/L4	156	132%	L3/L4	4445:D3	B	OK	OK	OK	OK	OK
826	4445	E3	166	122%	L3/L4/1AD/B!	162	137%	3AD/B	4445:E3	L4/#AD/B	<	OK	OK	OK	OK
827	4445	E5	158	116%	L2/L3	156	132%	L3/L4	4445:E5	L2	~B	OK	OK	OK	OK
828	4445	B6	152	112%	L2/L3	148	125%	L2/L3	4445:B6	#AD/B	<	OK	OK	OK	OK
829	4445	E6	158	116%	L1/L2	161	136%	L2/L3	4445:E6	L1/L2/L3	<	OK	OK	OK	OK
830	4445	B10	145	107%	L2	142	120%	L4/AD/B	4445:B10	L3/#AD/B!	<	OK	OK	OK	OK
										L1	L1	L1	~B	OK	OK
831	4445	C10	140	103%	L2/L3	133	113%	B	4445:C10	~B	OK	OK	OK	OK	OK
832	4445	E10	150	110%	L4/AD/B!	154	131%	L2/L3	4445:E10	Dead	#AD/B	OK	OK	OK	OK
833	4446	A4	133	98%	B!	134	114%	B!	4446:A4	L3/L4/#AD/E	~B	OK	OK	OK	OK
834	4446	D5	158	116%	L3/1AD/B!	150	127%	L3/L4/AD/B!	4446:D5	#AD/B	<	OK	OK	OK	OK
835	4446	D9	155	114%	L2/L3	138	117%	Dead	4446:D9	Dead	#AD/B	OK	OK	OK	OK
836	4447	A1	131	96%	L4/AD/B!	173	147%	L1/L2	4447:A1	<	OK	OK	OK	OK	OK
837	4447	C3	151	111%	L4/AD/B!	171	145%	B	4447:C3	~B	~B	OK	OK	OK	OK
										B!	B!	B!	OK	OK	OK
838	4447	D3	139	102%	2L4/2AD/B	166	141%	B	4447:D3	OK	OK	OK	OK	OK	OK
839	4447	D4	147	108%	L3/L4/AD/B! - No P, H	169	143%	L3/2AD/B!	4447:D4	L2/#AD/B!	<	OK	OK	OK	OK
840	4447	B5	137	101%	L3/L4	165	140%	L2/L3	4447:B5	L2/L3	OK	OK	OK	OK	OK
841	4447	C8	155	114%	B - Blebby	161	136%	L2/L3	4447:C8	L2/L3	<	<	OK	OK	OK
842	4448	A1	135	99%	L4/AD/B	123	104%	B	4448:A1	OK	OK	OK	OK	OK	OK
843	4448	C1	145	107%	L4/AD/B	140	119%	B!	4448:C1	OK	OK	OK	OK	OK	OK
844	4448	C4	146	107%	L3/L4/AD/B!	150	127%	L3/L4/AD/B! - Few Eggs	4448:C4	B	OK	OK	OK	OK	OK
										L1	L1	L1	OK	OK	OK
845	4448	C5	148	109%	B!	139	118%	L3/L4/AD/B! - No P, Few Eggs	4448:C5	OK	OK	OK	OK	OK	OK
846	4448	F4	170	125%	L4/AD/B!	144	122%	B	4448:F4	L4/#AD/B	<	OK	OK	OK	OK
847	4448	E5	151	111%	L2/L3/2AD/B!	138	117%	B	4448:E5	~B	OK	OK	OK	OK	OK
848	4448	D6	125	92%	B! - Unhatched Eggs	121	103%	B - Unhatched Eggs	4448:D6	~B	<	OK	OK	OK	OK

Table 3

849	4448	E6	152	112%	L3/L4	142	120%	B - Few Eggs	4448:E6	B	<	OK	OK	OK	OK
850	4448	F7	160	118%	L4/AD/B	123	104%	B	4448:F7	L4/#AD/B!	~B	<	OK	OK	OK
851	4448	C8	146	107%	L4/AD/B	146	124%	B	4448:C8	B	<	OK	OK	OK	OK
										B!	B!	B!	OK	OK	OK
852	4448	E9	142	104%	5AD/B	140	119%	B	4448:E9	Dead(L3)	OK	OK	OK	OK	OK
853	4448	F9	148	109%	L4/AD/B!	136	115%	B	4448:F9	Dead(L3)	OK	OK	OK	OK	OK
854	4448	B10	144	106%	B! - Healthy, Few Egg	128	108%	B!	4448:B10	#AD/B!	~B	OK	OK	OK	OK
855	4448	F10	148	109%	L1	153	130%	L1/L2	4448:F10	Dead(L3/L4)	~B	OK	OK	OK	OK
856	4448	H10	153	113%	1AD/B!	148	125%	L3	4448:H10	L3/L4/#AD/E	<	<	OK	OK	OK
857	4449	B3	150	110%	L3/L4/AD/B!	143	121%	B - Few Eggs	4449:B3	B	<	OK	OK	OK	OK
858	4449	C3	164	121%	L2	156	132%	L1/L2	4449:C3	L3/L4	OK	OK	OK	OK	OK
										L1	L1	L1	OK	OK	OK
859	4449	D3	145	107%	L2/L3/1AD/B!	145	123%	L2	4449:D3	#AD/B	OK	OK	OK	OK	OK
860	4449	E3	147	108%	L3/L4	151	128%	L2/L3	4449:E3	#AD/B	OK	OK	OK	OK	OK
861	4449	G3	161	118%	L3/L4	160	136%	L3/L4/AD/B! - Clear	4449:G3	L4/AD/B!	OK	OK	OK	OK	OK
862	4449	D4	137	101%	L2/L3	148	125%	L2/L3	4449:D4	#AD/B	OK	OK	OK	OK	OK
863	4449	G4	163	120%	L3/L4	154	131%	B!	4449:G4	#AD/B	OK	OK	OK	OK	OK
864	4449	C5	157	115%	L4/AD/B!	139	118%	B	4449:C5	B	OK	OK	OK	OK	OK
865	4449	E6	146	107%	L4/AD/B	144	122%	B	4449:E6	<	OK	OK	OK	OK	OK
										B!	B!	B!	OK	OK	OK
866	4449	B10	146	107%	L4/AD/B	146	124%	B	4449:B10	<	OK	OK	OK	OK	OK
867	4449	C10	153	113%	L3/L4	147	125%	L4/AD/B! - Clear	4449:C10	OK	OK	OK	OK	OK	OK
868	4449	D10	142	104%	L3	146	124%	L2/L3	4449:D10	B	OK	OK	OK	OK	OK
869	4449	E10	162	119%	L2/L3	155	131%	L2/L3	4449:E10	L2/L3	<	OK	OK	OK	OK
870	4449	D11	165	121%	L2/L3	151	128%	L3	4449:D11	#AD/B	OK	OK	OK	OK	OK
871	4450	E1	131	96%	L3/L4	140	119%	L4/AD/B	4450:E1	~B	OK	OK	OK	OK	OK
872	4450	C3	155	114%	L2/L3	168	142%	L3	4450:C3	B	OK	OK	OK	OK	OK
										L1	L1	L1	OK	OK	OK
873	4450	E3	148	109%	L2/L3	156	132%	L2/L3	4450:E3	B	OK	OK	OK	OK	OK
874	4450	F3	161	118%	L4/AD/B!	157	133%	B	4450:F3	~B	OK	OK	OK	OK	OK
875	4450	G3	148	109%	L4/AD/B!	131	111%	B	4450:G3	<	OK	OK	OK	OK	OK
876	4450	C4	148	109%	L2/L3	159	135%	L2	4450:C4	B	OK	OK	OK	OK	OK
877	4450	F5	152	112%	3AD/B	162	137%	L2/L3	4450:F5	L2	OK	OK	OK	OK	OK
878	4450	C6	148	109%	L1/L2	151	128%	L2	4450:C6	L1/L2	<	OK	OK	OK	OK
879	4450	E6	149	110%	L2/L3	153	130%	L2	4450:E6	L1/L2	OK	OK	OK	OK	OK
										B!	B!	B!	OK	OK	OK
880	4450	E10	145	107%	L1/L2	146	124%	2AD/B	4450:E10	#AD/B	OK	OK	OK	OK	OK
881	4450	F10	153	113%	L2/L3	153	130%	L2/L3	4450:F10	#AD/B	OK	OK	OK	OK	OK
882	4451	A4	136	100%	B!	142	120%	L3/2AD/B!	4451:A4	#AD/B	~B	~B	~B	<	OK
883	4451	B9	141	104%	Dead	156	132%	Dead	4451:B9	L1/Dead(L2)	#AD/B	<	OK	OK	OK
884	4451	B10	149	110%	L3	152	129%	L2/L3	4451:B10	Dead(L3)/#A	#AD/B	OK	OK	OK	OK
885	4451	C10	150	110%	L3	150	127%	Dead	4451:C10	L2/L3	~B	~B	OK	OK	OK
886	4451	D10	138	101%	L3/4AD/B!	133	113%	B!	4451:D10	#AD/B	B	OK	OK	OK	OK
										L1	L1	L1/L2	#AD/~B	OK	OK
887	4452	D4	138	101%	B!	133	113%	B - 1/3 clear Spot	4452:D4	L3/#AD/B!	OK	OK	OK	OK	OK
888	4452	A5	128	94%	4AD/B!	129	109%	L3/L4 - Dying	4452:A5	L2	L2	<	OK	OK	OK
889	4452	B7	146	107%	2AD/B	149	126%	Dead (L3)	4452:B7	Dead	<	OK	OK	OK	OK
890	4452	A9	135	99%	L2/L3	128	108%	L2/L3	4452:A9	L1/L2	#AD/B	#AD/B	OK	OK	OK

Table 3

891	4452	B9	151	111%	L2/L3	144	122%	L2/L3	4452:B9	#AD/B	~B	<	OK	OK	OK
892	4452	D9	144	106%	L2/L3	145	123%	L2/L3	4452:D9	L2/L3	~B	OK	OK	OK	OK
893	4452	E9	133	98%	4AD/B	141	119%	B	4452:E9	#AD/B	<	<	OK	OK	OK
										B!	B!	B!	OK	OK	OK
894	4452	B10	149	110%	L1/L2	143	121%	Dead	4452:B10	Dead	Dead	OK	OK	OK	OK
895	4452	C10	146	107%	Dead	140	119%	Dead (L3)	4452:C10	Dead(L3)	<	OK	OK	OK	OK
896	4452	A11	125	92%	L2/L3	127	108%	L2/L3	4452:A11	L1/L2	~B	OK	OK	OK	OK
897	4452	B11	145	107%	L2/L3	150	127%	L3/L4 - Husks	4452:B11	L2	<	OK	OK	OK	OK
898	4452	D11	138	101%	L2/L3	144	122%	L2	4452:D11	L1/L2	#AD/B	<	OK	OK	OK
899	4455	E9	151	111%	L2/L3	154	131%	L2	4455:E9	L1/L2	OK	OK	OK	OK	OK
900	4456	A4	140	103%	L2/L3	174	147%	B	4456:A4	#AD/B!	#AD/B	B	~B	OK	OK
										L1	L1	L1	~B	OK	OK
901	4456	H4	166	122%	L3/L4/AD/B!	190	161%	L4/AD/B! - Clear, Few Eggs	4456:H4	~B	OK	OK	OK	OK	OK
902	4456	C5	153	113%	L3/L4/AD/B!	147	125%	L4/AD/B	4456:C5	OK	OK	OK	OK	OK	OK
903	4456	D5	150	110%	L1/L2	172	146%	L2/L3	4456:D5	Dead(L3)	#AD/B	~B	OK	OK	OK
904	4456	H5	153	113%	L3/1AD/B	187	158%	L3/L4/AD/B!	4456:H5	<	OK	OK	OK	OK	OK
905	4456	H6	161	118%	L2/L3	168	142%	L4/AD/B!	4456:H6	~B	<	OK	OK	OK	OK
906	4456	D9	141	104%	L2/L3 - Husks	153	130%	3AD/B	4456:D9	#AD/B	OK	OK	OK	OK	OK
907	4456	B10	136	100%	L4/AD/B! - Healthy, F	144	122%	B! - No P, Healthy, Few Eggs	4456:B10	OK	<	<	OK	OK	OK
										B!	B!	B!	OK	OK	OK
908	4456	D10	143	105%	L2/L3	162	137%	L3/L4	4456:D10	B	<	OK	OK	OK	OK
909	4456	E11	157	115%	L2/L3	159	135%	L4/AD/B! - Clear	4456:E11	B	OK	OK	OK	OK	OK
910	4456	F11	158	116%	L4/AD/B	151	128%	B	4456:F11	~B	OK	OK	OK	OK	OK
911	4457	A1	139	102%	L1/L2	181	153%	L2	4457:A1	L2/L3	~B	OK	OK	OK	OK
912	4457	B1	149	110%	L3/L4	173	147%	B	4457:B1	#AD/~B	OK	OK	OK	OK	OK
913	4457	C8	141	104%	Dead	151	128%	L2	4457:C8	Dead(L2/L3)	#AD/B	<	OK	OK	OK
914	4457	D10	154	113%	L3/L4/AD/B!	155	131%	B	4457:D10	#AD/B	<	<	OK	OK	OK
										L1	L1	10	OK	OK	B!
915	4458	D4	146	107%	L3/L4	145	123%	L4/AD/B! - No P, Clear	4458:D4	B	OK	OK	OK	OK	OK
916	4458	A5	139	102%	L1/L2	132	112%	L3	4458:A5	L1/L2	L1/L2	L1/L2/L3	#AD/B!	OK	OK
917	4458	D5	147	108%	L2/L3	140	119%	L4/AD/B!	4458:D5	#AD/B	#AD/B	OK	OK	OK	OK
918	4458	A8	136	100%	L3/2AD/B!	126	107%	L2	4458:A8	Dead	#AD/~B	<	OK	OK	OK
919	4458	C8	142	104%	1AD/B	139	118%	3AD/B	4458:C8	L2	#AD/~B	OK	OK	OK	OK
920	4458	A9	125	92%	5AD/B	122	103%	5AD/B	4458:A9	#AD/B	#AD/B	~B	B	OK	OK
921	4458	H9	168	124%	L4/AD/B	154	131%	L4/AD/B	4458:H9	#AD/B	<	OK	OK	OK	OK
										B!	B!	OK	OK	OK	OK
922	4458	D10	147	108%	L3	137	116%	L3	4458:D10	~B	OK	OK	OK	OK	OK
923	4458	D11	152	112%	L1/L2	143	121%	L2/L3	4458:D11	L2/Dead(L3)	L2/Dead(L	L3/L4	<	OK	OK
924	4459	B10	149	110%	4AD/B	140	119%	L3/L4/AD/B!	4459:B10	B	<	OK	OK	OK	OK
925	4459	C10	155	114%	B!	125	106%	B	4459:C10	B	OK	OK	OK	OK	OK
926	4459	D11	154	113%	L2/L3	147	125%	L3/L4/AD/B!	4459:D11	~B	OK	OK	OK	OK	OK
927	4460	C4	157	115%	L1/L2	150	127%	L2/L3	4460:C4	#AD/B	OK	OK	OK	OK	OK
928	4461	C4	151	111%	L4/AD/B!	133	113%	B	4461:C4	<	<	OK	OK	OK	OK
										L1	L1	L1	OK	OK	OK
929	4461	C9	142	104%	L4/AD/B	121	103%	B	4461:C9	~B	<	OK	OK	OK	OK
930	4464	A5	136	100%	L2	144	122%	L2/L3	4464:A5	L2/L3	L3	~B	OK	OK	OK
931	4464	D5	146	107%	L2/L3	147	125%	L3	4464:D5	#AD/B	OK	OK	OK	OK	OK
932	4464	A8	119	88%	2AD/B	118	100%	B	4464:A8	#AD/B	OK	OK	OK	OK	OK

Table 3

933	4464	C8	141		104%	L1/L2/L3	150	127%	L2/L3	4464:C8	L1/L2	L2/Dead(L	#AD/B	OK	OK	OK
934	4464	D8	156		115%	L2/L3	166	141%	L3	4464:D8	L1/L2	L2/L3	<	OK	OK	OK
935	4464	B10	152		112%	L2/L3	145	123%	L3/L4	4464:B10	#AD/B	OK	OK	OK	OK	OK
											B!	B!	B!	OK	OK	OK
936	4464	D10	149		110%	L3/L4	140	119%	L3	4464:D10	#AD/B	OK	OK	OK	OK	OK
937	4466	E11	147		108%	L4/AD/B	133	113%	B	4466:E11	<	OK	OK	OK	OK	OK
938	4467	E8	165		121%	L2	158	134%	L2	4467:E8	L1/L2	L2/L3	L2/L3	<	OK	OK
939	4468	C1	156		115%	L1/L2	149	126%	L3	4468:C1	#AD/B	B	OK	OK	OK	OK
940	4468	D9	146		107%	L4/AD/B! - No P	135	114%	B	4468:D9	#AD/B	#AD/B	OK	OK	OK	OK
941	4468	C10	156		115%	L2	143	121%	L3/L4/AD/B! - No P, No Eggs	4468:C10	B!	~B	~B	OK	OK	OK
942	4469	C8	146		107%	2L4/2AD/B! - Husks	143	121%	Dead (AD)	4469:C8	L1/L2	L2/Dead(L<		OK	OK	OK
											L1	L1	L1	~B	OK	OK
943	4470	B6	147		108%	L3/L4	143	121%	L1/L2/L3	4470:B6	L4/#AD/B!	B!	~B	OK	OK	OK
944	4470	D6	140		103%	L3/L4/AD/B!	125	106%	B	4470:D6	L2/L3/L4	<	OK	OK	OK	OK
945	4470	B10	149		110%	L2/L3	140	119%	L4/AD/B! - No P	4470:B10	#AD/B!	#AD/B	OK	OK	OK	OK
946	4470	C10	155		114%	L2/L3	141	119%	L2/L3	4470:C10	L2/L3	#AD/B!	~B	OK	OK	OK
103	4470	D10	150		110%	L1/L2	139	118%	L2/L3	4470:D10	L1/L2	Dead(L3/L	Dead(L4)	B	L4/#AD/B<	
947	4470	E10	148		109%	L2/L3	136	115%	L2/L3	4470:E10	L3/#AD/B!	~B	OK	OK	OK	OK
948	4470	C11	142		104%	L3/L4	139	118%	L4/1AD/B! - Dying	4470:C11	L4/#AD/B!	<	<	OK	OK	OK
											B!	B!	B!	OK	OK	OK
949	4470	D11	152		112%	L2/L3	134	114%	2L4/1AD/B! - No P	4470:D11	L1/L2	L2	OK	OK	OK	OK
950	4471	F10	143		105%	B! - Healthy, Few Egg	122	103%	B - Healthy, Few Eggs	4471:F10	OK	OK	OK	OK	~B	OK
951	4473	D3	149		110%	L3/L4/1AD/B!	156	132%	L1/L2	4473:D3	OK	OK	OK	OK	OK	OK
952	4473	E7	154		113%	L3/L4	157	133%	4AD/B	4473:E7	Dead(L3/L4)	L4/B	OK	OK	OK	OK
953	4473	E9	154		113%	L2/L3	150	127%	L3/L4	4473:E9	L3/#AD/B!	OK	OK	OK	OK	OK
954	4473	E10	156		115%	L2/L3	147	125%	L2/L3	4473:E10	L2	<	OK	OK	OK	OK
955	4476	C7	136		100%	2AD/B	142	120%	3AD/B	4476:C7	L2/Dead(L3)	#AD/B	#AD/B	OK	OK	OK
											L1	L1	L1	OK	OK	OK
956	4476	B10	151		111%	L2	151	128%	L2/L3	4476:B10	L1/L2	L2/L3	-B	OK	OK	OK
957	4476	C10	143		105%	L3/2AD/B!	141	119%	2AD/B	4476:C10	Dead(L2/L3)	#AD/B	#AD/~B	OK	OK	OK
958	4476	D10	149		110%	L3/L4	150	127%	L2	4476:D10	#AD/B!	#AD/~B	-B	OK	OK	OK
959	4476	A11	132		97%	L1/L2	128	108%	L2	4476:A11	L1	L2/Dead(L	L2/L3	#AD/B	OK	OK
960	4476	D11	151		111%	L2	143	121%	L3	4476:D11	L2/L3	L4/#AD/B!	<	OK	OK	OK
961	4480	D5	166		122%	Dead	151	128%	L2	4480:D5	Dead(L3)	B	<	OK	OK	OK
962	4480	B7	139		102%	B! - Few Eggs	113	96%	B! - Healthy	4480:B7	L4/#AD/B!	B	OK	OK	OK	OK
											B!	B!	B!	OK	OK	OK
963	4480	A9	125		92%	L3/L4	129	109%	L3	4480:A9	B	OK	OK	OK	OK	OK
964	4480	D9	146		107%	Dead (L2/L3)	144	122%	Dead (L3)	4480:D9	Dead(L4)	OK	OK	OK	OK	OK
965	4481	D5	157		115%	L3/L4	162	137%	L2	4481:D5	L4/AD/B!	<	OK	OK	OK	OK
966	4481	D10	159		117%	L1/L2	160	136%	L2	4481:D10	L1	L1/L2	L1/L2	#AD/B	~B	OK
967	4482	D5	157		115%	L2	156	132%	L1/L2	4482:D5	L2	B	OK	OK	OK	OK
968	4482	D10	131		96%	Dead	134	114%	Dead(L3)	4482:D10	Dead(L3)	OK	OK	OK	OK	OK
969	4482	A11	126		93%	Dead	118	100%	Dead	4482:A11	L1	~B	OK	OK	OK	OK
											L1	L1	L1	<	OK	OK
970	4482	D11	146		107%	L2	136	115%	L2	4482:D11	L2/L3	OK	OK	OK	OK	OK
971	4484	E10	153		113%	L2/L3	150	127%	L3/L4/AD/B!	4484:E10	L2/L3	OK	OK	OK	OK	OK
972	4484	E11	147		108%	L3/L4	131	111%	B!	4484:E11	L4/#AD/B!	OK	OK	OK	OK	OK
973	4486	A4	144		106%	L3/L4/AD/B!	124	105%	L3/L4	4486:A4	B	OK	OK	OK	OK	OK

Table 3

974	4487	A1	129	95%	L2/L3/L4	125	106%	L3/L4	4487:A1	B	OK	OK	OK	OK	OK
975	4487	B1	133	98%	L4/AD/B	138	117%	B	4487:B1	B	OK	OK	OK	OK	OK
976	4487	B2	133	98%	L4/AD/B	120	102%	B	4487:B2	~B	OK	OK	OK	OK	OK
										B!	B!	B!	OK	OK	OK
977	4488	B9	151	111%	L3/L4	140	119%	L3/L4	4488:B9	L1/L2	OK	OK	OK	OK	OK
978	4488	A10	129	95%	3AD/B!	114	97%	L3	4488:A10	L1/L2	B	OK	OK	OK	OK
979	4488	C10	141	104%	1AD/~B	124	105%	3AD/B	4488:C10	#AD/B	OK	OK	OK	OK	OK
980	4488	D10	145	107%	L2/L3	133	113%	L3/L4	4488:D10	#AD/B!	OK	OK	OK	OK	OK
981	4493	A1	138	101%	L3/L4	122	103%	B	4493:A1	#AD/B	OK	OK	OK	OK	OK
982	4493	B9	152	112%	L2/L3	126	107%	~B	4493:B9	Dead(L4)	#AD/B	OK	OK	OK	OK
983	4494	A1	126	93%	L3/L4	109	92%	B	4494:A1	OK	OK	OK	OK	OK	OK
										L1	L1	L1	OK	OK	OK
984	4494	B1	129	95%	L2/L3/L4	125	106%	L4/AD/B!	4494:B1	#AD/B	OK	OK	OK	OK	OK
985	4494	C10	139	102%	L2	133	113%	1AD/B - L4/AD Husks	4494:C10	Dead(L2/L3)	OK	OK	OK	OK	OK
986	4494	A11	130	96%	Dead	123	104%	Dead	4494:A11	Dead	L1/L2	OK	OK	OK	OK
987	4494	H11	157	115%	L3	167	142%	B	4494:H11	Dead(L2)	#AD/B	OK	OK	OK	OK

Example 8 – Sheep Test I Experimental Procedure

Sheep naturally infected with a variety of gastrointestinal nematodes are purchased from local sources and are transported to the test site. The animals are housed in a manner to preclude further infection by nematode larvae. The animals are evaluated for the presence of adequate nematode burdens by performing a standard fecal egg per gram (EPG) count. Eggs are differentiated into the following groups: trichostrongyle (strongyle), Strongyloides, Trichuris, or Nematodinis. Only sheep judged by the study parasitologist to have adequate nematode infections are retained as test subjects.

The sheep are fed good quality hay (no concentrated rations) and water ad libitum. Following a five-day acclimation period, the sheep are randomly assigned by EPG count into treatment groups which include non-treated Negative control (placebo); Positive Control (commercially available ivermectin for sheep): and various anthelmintic compounds of the present invention (test compound) dissolved in DMSO. The first replicate of 10 animals is randomly assigned to groups 1-10; the second replicate of 10 animals is randomly assigned to groups 1-10; and the third replicate of 10 animals is randomly assigned to groups 1-10. Thus 10 groups of 3 animals each is created.

The randomization is performed on fecal samples collected 24-48 hours prior to scheduled treatment. The EPG counts are performed according to Zimmerman Research SOP # NMEPG.99.01

On treatment day, the animals are weighed and divided into groups with three animals per group as follows:

GROUP 1: Non-treated negative control (placebo) of 10 ml of DMSO.
GROUP 2: Positive Control treatment of 200 mcg/kg commercially available ivermectin for sheep.
GROUP 3: Compound @ dissolved in DMSO.
GROUP 4: Compound @ dissolved in DMSO.
GROUP 5: Compound @ dissolved in DMSO.
GROUP 6: Compound @ dissolved in DMSO.
GROUP 7: Compound @ dissolved in DMSO.
GROUP 8: Compound @ dissolved in DMSO.
GROUP 9: Compound @ dissolved in DMSO.

GROUP10: Compound @ dissolved in DMSO.

The placebo (DMSO), the commercially available drug, and the test anthelmintic compounds are administered in a 3ml volume by subcutaneous injection using a sterile syringe fitted with a proper needle. The animal is adequately immobilized for injection of the placebo, commercially available drug, or test anthelmintic compound.

Following treatment, the animals are observed at hourly intervals for the first 8 hours, then daily until necropsy. They will continue to be housed in a manner to prevent further nematode infections. Fecal samples are taken for EPG counts on the 5th day and 7th day after treatment.

Seven days following treatment the sheep are humanely slaughtered in accordance with the Guide for the Care and Use of Laboratory Animals (DHEW Publication No. 86-23). Necropsy procedures are according to Zimmerman Research SOP # NCRGIH.99.01, Necropsy for Helminth Recovery, specifically for gastrointestinal nematodes. Fecal samples are taken for EPG counts during the sample collection process on this day. All animals are necropsied, but only the animals from the experimental treatment groups that have a significant egg count reduction on day 5 or day 7 will have intestinal material collected for nematode recovery and identification.

Nematodes are recovered, identified, and enumerated according to Zimmerman Research SOP # NEMRECOVID.99.01. All individuals performing nematode recoveries are blinded to treatment versus control animals. Preliminary estimates of total nematodes recovered from each gut sample are provided prior to identification and enumerations by the study parasitologist. At the discretion of the study parasitologist, seven days after the drug administration fecal egg counts are performed and all animals showing 90% or better trichostrongylid egg reduction will be slaughtered using humane methods recommended by the AVMA. The neck blood vessels are severed and after the animal is completely exsanguinated, the abdomen are opened. The abomasum, the small and large intestines are tied at the omasal and pyloric openings, the duodenum, the end of the small intestine and at the end of the large intestine. Each section is transferred in a separate bucket containing warm water and is slit open and thoroughly washed. The epithelium is inspected before it is removed. The thus prepared washings are saved in gallon jars. An appropriate preservative is added. If preservative is not available, all the intestinal washing

should kept in a refrigerator. These washings are passed through a 100-mesh sieve (pore size 149 pm), and the residue is examined for the presence of worms under a dissecting microscope, Lugol's solution may be used to stain the worms. All worms are picked up counted and identified as to the species. An effort should be made to recover any immature forms present. The efficacy should be calculated using the controlled anthelmintic test.

$$\text{Percentage efficacy} = \frac{\text{(Mean number of worms in controls minus Mean number of worms in treated animal)}}{\text{Mean number of worms in controls}} \times 100$$

Results are depicted in Tables 4 and 5.

Table 4

Akkadix	**AKK 101**	Sheep	Trial	17-Jan				
		Rumen	Injection					
	Sheep	Weight/lbs		**Worm**	**Counts**			
	Number	1/17/2000	Abomasum	Abomasum	Small Intestine	Small Intest.		
			Haemonchus	Ostertagia	Trichostrongylus	Nematodirus		
Group	81	84	420	60	0	140		
Negative	75	116	500	860	320	2300		
Control	56	87	0	0	80	0		
Mean Ct.			307	307	133	813		
Group	83	98	0	0	0	0		
Ivermectin	92	129	0	0	0	0		
200mcg/kg	53	82	0	0	0	0		
Mean Ct.			0	0	0	0		
		%Efficacy	**100**	**100**	**100**	**100**		
		%Efficacy	**#REF!**					
Group	63	84	0	0	520	2640		
AKC 103	76	110	0	0	880	240		
1mg/kg	62	80	0	20	0	0		
Mean Ct.			0	7	467	960		
		%Efficacy	**100**	**98**				

Table 5

Akkadix	Trial -1	Sheep	**AKK 101**	Strongyles	Strongyles		Strongyles	
	Sheep	Weight/lbs	Total	17-Jan	22-Jan		24-Jan	
	Number	1/12/2000	EPG-pre	EPG-pre	EPG-5day	% Change	EPG-7day	%Change
Group 1	63	80	3160	3110	60		70	97.75
AKC 103	76	101	410	410	190		980	-139.02
1.4mg/kg	62	76	120	80	0		0	100.00
Total / Mean		257	1230.00	1200.00	83.33	93.06	350.00	**70.83**
Group 9	83	91	2310	2000	10		0	100.00
Ivermectin	92	113	570	570	0		0	100.00
.2mg/kg	53	77	90	70	0		0	100.00
Total / Mean		281	990.00	880.00	3.33	99.62	0.00	**100.00**
Group 10	81	74	2240	2240	780		770	65.63
Negative	75	109	370	300	260		1360	-353.33
Control	56	80	40	40	30		30	25.00
Total / Mean		263	883.33	860.00	356.67	58.53	720.00	**16.28**

Example 9 – Sheep Test II Experimental Procedure

Sheep naturally infected with a variety of gastrointestinal nematodes are purchased from local sources and are transported to the test site. The animals are housed in a manner to preclude further infection by nematode larvae. The animals are evaluated for the presence of adequate nematode burdens by performing a standard fecal egg per gram (EPG) count. Eggs are differentiated into the following groups: trichostrongyle (strongyle), Strongyloides, Trichuris, or Nematodiris. Only sheep judged by the study parasitologist to have adequate nematode infections are retained as test subjects.

The sheep are fed good quality hay (no concentrated rations) and water ad libitum. Following a five day acclimation period, the sheep are randomly assigned by EPG count into the following treatment groups: Groups 1-9, various anthelmintic compounds of the present invention (test compound) dissolved in DMSO: Group 10, Positive Control (commercially available ivermectin for sheep); Group 11, non-treated Negative control (DMSO only). The first replicate of 11 animals is randomly assigned to groups 1-11; the second replicate of 11 animals is randomly assigned to groups 1-11; and the third replicate of 11 animals is randomly assigned to groups 1-11. Thus 11 groups of 3 animals each are created.

The randomization is performed on fecal samples collected 24-48 hours prior to scheduled treatment. The EPG counts are performed according to Zimmerman Research SOP # NMEPG.99.01.

GROUP 1: AKKADIX compound dissolved in DMSO.
GROUP 2: AKKADIX compound dissolved in DMSO.
GROUP 3: AKKADIX compound dissolved in DMSO.
GROUP 4: AKKADIX compound dissolved in DMSO.
GROUP 5: AKKADIX compound dissolved in DMSO.
GROUP 6: AKKADIX compound dissolved in DMSO.
GROUP 7: AKKADIX compound dissolved in DMSO.
GROUP 8: AKKADIX compound dissolved in DMSO.
GROUP 9: AKKADIX compound dissolved in DMSO.
GROUP 10: Positive Control treatment of 200 mcg/kg commercially available ivermectin for sheep.

GROUP11: Non-treated negative control (placebo) of 3 ml of DMSO.

On treatment day, the animals are weighed, tagged, and divided into groups of three animals per group as follows:

The placebo (DMSO), the commercially available drug, and the test anthelmintic compounds are administered in a 3ml volume of DMSO by subcutaneous injection using a sterile syringe fitted with a sterile needle. The site of injection is clipped and swabbed with alcohol prior to injection. The animal is adequately immobilized for injection of the placebo, commercially available drug, or experimental compound.

Following treatment, the animals are observed at hourly intervals for the first 8 hours, then daily until necropsy. They are housed in a manner to prevent further nematode infections.

On the fifth day following treatment, fecal samples are obtained from each animal, properly labeled and used for EPG counts.

Seven days following treatment, all the sheep are weighed and humanely slaughtered in accordance with the Guide for the Care and Use of Laboratory Animals (DHEW Publication No. 86-23). Necropsy procedures are according to Zimmerman Research SOP # NCRGIH.00.01, Necropsy for Helminth Recovery, specifically for gastrointestinal nematodes. Fecal samples are taken for EPG counts during the sample collection process on this day.

Nematodes are recovered, identified, and enumerated according to Zimmerman Research SOP # NEMRECOVID.00.01. All individuals performing nematode recoveries are blinded to treatment versus control animals.

Anthelmintic efficacy is calculated using the controlled test procedure:

$$\% \text{ Efficacy} = \frac{\text{Mean number of worms in controls minus mean number of worms in treated}}{\text{Mean number of worms in controls}} \times 100$$

Results are depicted in Tables 6 and 7.

Table 6

Akkadix	AKK-102	Sheep	24-May						
	Sheep	Weight/lbs		Worm	Counts				
	Number	5/17/2000	Abomasum	Abomasum	Small Intestine		Small Intest.	Large Intest.	
			Haemonchus	Ostertagia	Trichostrongylus		Nematodirus	Trichuris	
Group	530	47	60	580	40		8500	5	
Negative	1341	57	60	20	20		2520	15	
Control	524	54	20	80	0		0	10	
Mean Ct.			47	227	20		3673	10	
Group	1347	45	0	0	0		100	0	
Ivermectin	1336	58	20	0	0		100	0	
200mcg/kg	539	47	0	0	0		0	0	
Mean Ct.			7	0	0		67	0	
		%Efficacy	**86**	**100**	**100**		**98**		
Group	525	35	40	1540	120		9320	10	
AKC 103	522	30	80	500	40		5780	20	
1mg/kg	1333	37	0	400	140		7920	20	
Mean Ct.			40	813	100		7673	17	
		%Efficacy	**14**						

Table 7

Akkadix	Trial -2	Sheep	**AKK 102**	Strongyles	Strongyles		Strongyles	
	Sheep	Weight/lbs	Total	15-May	22-May		24-May	
	Number	5/17/2000	EPG-pre	EPG-pre	EPG-5day	% Change	EPG-7day	%Change
Group 1	525	35	1850	1430	460		690	51.75
AKC 103	522	30	470	360	670		180	50.00
1mg/kg	1333	37	160	130	100		240	-84.62
Total / Mean		102	826.67	640.00	410.00	35.94	370.00	**42.19**
Group 2	1347	45	560	450	0		0	100.00
Ivermectin	1336	58	220	170	0		0	100.00
200mcg/kg	539	47	100	40	0		0	100.00
Total / Mean		150	293.33	220.00	0.00	100.00	0.00	**100.00**

It should be understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application and the scope of the appended claims.

Table 8

Hydroxyamidines.

The quantities specified below are for a set of six plates according to the library layout. 380 mL of a 0.2 M solution of each hydroxyamidine is required for each set of plates.

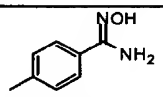
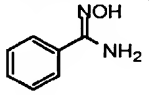
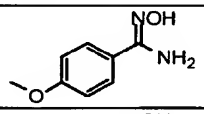
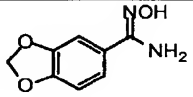
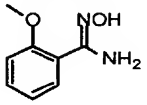
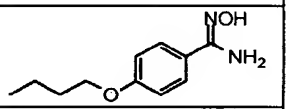
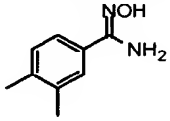
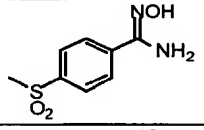
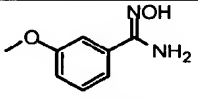
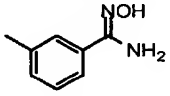
Entry	ACD	MW	Amt. (g)	Name	Structure
1	19952	150	11.4	4-methylbenzamidoxime	
2	31485	136	10.34	benzamidoxime	
3	NA	166	12.62	4-methoxybenzamidoxime	
4	119015	180	13.68	piperonyloamidoxime	
5	NA	166	12.62	2-methoxybenzamidoxime	
6	NA	208	15.81	4-n-butoxybenzamidoxime	
7	NA	164	12.46	3,4-dimethylbenzamidoxime	
8	NA	214	16.26	4-methylsulfonylbenzamidoxime	
9	NA	166	12.62	3-methoxybenzamidoxime	
10	NA	150	11.4	3- methylbenzamidoxime	

Table 9

BOC-amino acids

The quantities specified below are for a set of six plates according to the library layout. 30 mL of a 0.2 M solution of each BOC-amino acid is required for each set of plates.

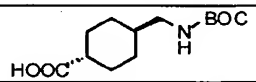
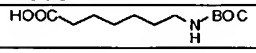
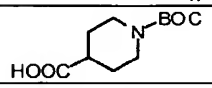
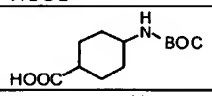
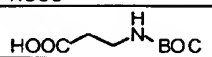
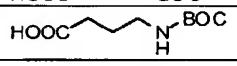
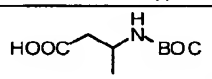
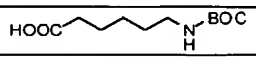
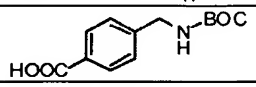
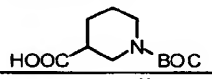
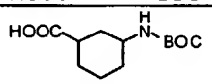
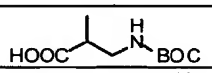
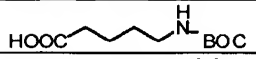
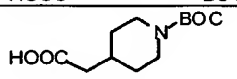
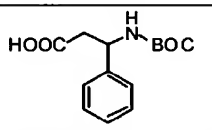
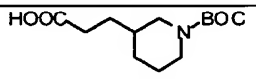
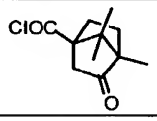
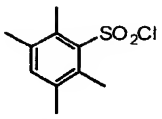
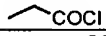
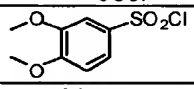
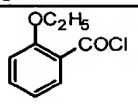
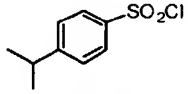
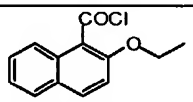
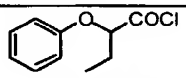
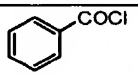
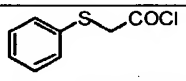
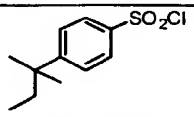
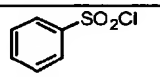
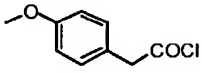
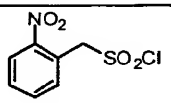
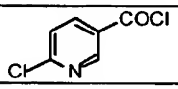
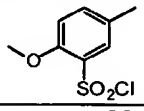
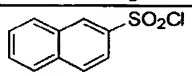
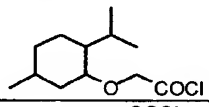
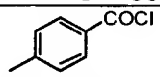
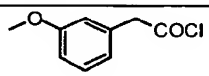
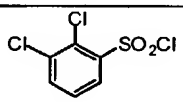
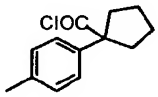
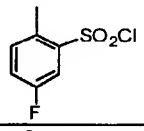
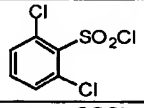
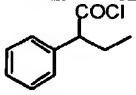
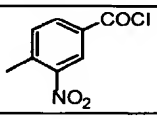
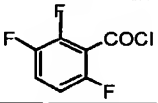
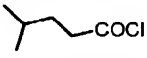
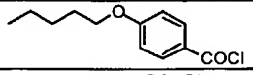
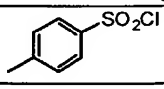
Entry	ACD	MW	Amt. (g)	Name	Structure
1	NA	257	1.542	BOC-trans-4-(aminomethyl) cyclohexanecarboxylic acid	
2	63356	245	1.47	BOC-7-aminoheptanoic acid	
3	76999	229	1.374	BOC-isonipecotic acid	
4	NA	243	1.458	BOC-4-aminocyclohexane carboxylic acid (cis/trans mixture)	
5	37291	189	1.134	BOC-beta-Ala-OH	
6	37313	203	1.218	BOC-4-aminobutyric acid	
7	270338	203	1.218	BOC-DL-3-aminobutyric acid	
8	37798	231	1.386	BOC-6-aminohexanoic acid	
9	228182	251	1.506	BOC-4-(aminomethyl)benzoic acid	
10	NA	229	1.374	BOC-nipecotic aicd	
11	NA	243	1.458	BOC-3-aminocyclohexane carboxylic acid (stereochemistry undefined)	
12	NA	203	1.218	BOC-DL-beta-aminobutyric acid	
13	76903	217	1.302	BOC-5-aminopentanoic acid	
14	NA	243	1.458	BOC-4-piperidinoacetic acid	
15	NA	265	1.59	Boc-DL-3-amino-3-phenylpropionic acid	
16	NA	257	1.542	BOC-3-(3-piperidino)propionic acid	

Table 10

Acylators

The quantities specified below are for a set of six plates according to the library layout. 17 mL of a 0.15 M solution of each acylator is required for each set of plates.

Entry	ACD	MW	Amt. (g)	Name	Structure
1	135626	216	0.552	(-)-Camphanic acid chloride	
2	14723	232	0.593	2,3,5,6-Tetramethylbenzene sulfonyl chloride	
3	745	92	0.236	propionyl chloride	
4	51769	236	0.604	3,4-dimethoxybenzenesulfonyl chloride	
5	16348	184	0.469	o-Ethoxybenzoyl chloride	
6	41510	218	0.558	4-isopropylbenzenesulfonyl chloride	
7	46426	234	0.598	2-ethoxy-1-naphthoyl chloride	
8	51569	198	0.507	2-phenoxybutyryl chloride	
9	653	140	0.358	benzoyl chloride	
10	54471	186	0.476	(phenylthio)acetyl chloride	
11	41509	246	0.629	4-t-amylbenzenesulfonyl chloride	
12	7426	176	0.450	benzenesulfonyl chloride	
13	75474	184	0.471	4-methoxyphenylacetyl chloride	
14	82526	235	0.601	2-nitro-alpha-toluenesulfonyl chloride	

Entry	ACD	MW	Amt. (g)	Name	Structure
15	51775	176	0.449	6-chloronicotinyl chloride	
16	60552	220	0.563	6-methoxy-m-toluenesulfonyl chloride	
17	4087	219	0.558	2-Naphthalenesulfonyl chloride	
18	44947	232	0.594	(-)-menthoxyacetyl chloride	
19	696	154	0.394	p-toluoyl chloride	
20	12244	184	0.471	3-methoxyphenylacetyl chloride	
21	51844	245	0.626	2,3-dichlorobenzenesulfonyl chloride	
22	44899	243	0.620	1-(4-chlorophenyl)-1-cyclopentanecarbonyl chloride	
23	52958	208	0.532	5-fluoro-3-methylbenzene sulfonyl chloride	
24	59482	138	0.353	3-methylthiopropionyl chloride	
25	52311	245	0.626	2,6-dichlorobenzenesulfonyl chloride	
26	18811	182	0.466	2-phenylbutyryl chloride	
27	35747	199	0.509	4-methyl-3-nitrobenzoyl chloride	
28	61203	194	0.496	2,3,6-trifluorobenzoyl chloride	
29	18814	134	0.343	gamma-methylvaleroyl chloride	
30	41723	226	0.578	4-N-amyloxybenzoyl chloride	
31	7450	190	0.486	p-toluenesulfonyl chloride	

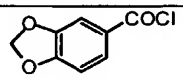
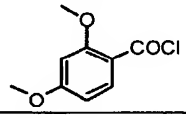
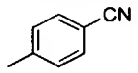
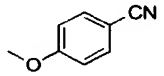
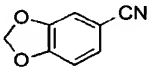
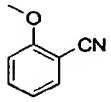
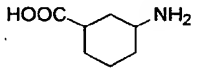
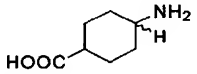
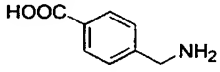
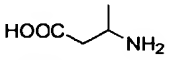
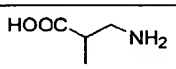
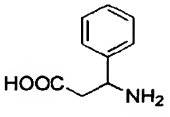
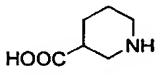
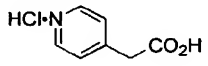
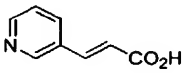
Entry	ACD	MW	Amt. (g)	Name	Structure
32	16904	184	0.471	piperonyloyl chloride	
33	17527	200	0.512	2,4-dimethoxybenzoyl chloride	

Table 11

Commercially available building blocks

for the preparation of the Hydroxyamidines and BOC-amino acids.

Entry	ACD	MW	Name	Structure
1	1827	117	p-tolunitrile	
2	1818	133	4-methoxybenzonitrile	
3	5820	147	piperonylonitrile	
4	1783	133	2-methoxybenzonitrile	
5	43482	208	4-n-butoxybenzonitrile	□
6	16380	164	3,4-dimethybenzonitrile	□
7	216489	214	4-methylsulfonylbenzonitrile	□
8	1801	166	3-methoxybenzonitrile	□
9	1808	117	m-tolunitrile	□
10	1466	157	trans-4-(aminomethyl) cyclohexanecarboxylic acid	□
11	6004	129	isonipecotic acid	□
12	59562	143	3-aminocyclohexanecarboxylic acid (stereochemistry undefined)	
13	191601	143	4-aminocyclohexanecarboxylic acid (cis/trans mixture)	
14	10203	151	4-(aminomethyl)benzoic acid	
15	8087	103	DL-3-Aminobutyric acid	
16	8145	103	DL-β-Aminoisobutyric acid	
17	8064	165	DL-3-Phenylpropionic acid	

Entry	ACD	MW	Name	Structure
18	5992	129	DL-Nipecotic acid	
19	12827	174	4-Pyridylacetic acid hydrochloride	
20	6410	149	Trans-3-(3-Pyridyl)acrylic acid	

Claims

What is claimed is:

1. A method for controlling nematodes which comprises contacting said nematodes with a nematode-controlling effective amount of a composition comprising at least one compound having Structure 47.

2. A method for controlling nematodes which comprises contacting said nematodes with a nematode-controlling effective amount of a composition comprising at least one compound having a structure selected from the group consisting of Structures 24 and 48-226.

3. The method of claim 2, wherein said compound is Compound 24.

4. The method of claim 2, wherein said compound is Compound 48.

5. The method of claim 2, wherein said compound is Compound 49.

6. The method of claim 2, wherein said compound is Compound 50.

7. The method of claim 2, wherein said compound is Compound 51.

8. The method of claim 2, wherein said compound is Compound 52.

9. The method of claim 2, wherein said compound is Compound 53.

10. The method of claim 2, wherein said compound is Compound 54.

11. The method of claim 2, wherein said compound is Compound 55.

12. The method of claim 2, wherein said compound is Compound 56.

13. The method of claim 2, wherein said compound is Compound 57.

14. The method of claim 2, wherein said compound is Compound 58.

15. The method of claim 2, wherein said compound is Compound 59.

16. The method of claim 2, wherein said compound is Compound 60.

17. The method of claim 2, wherein said compound is Compound 61.

18. The method of claim 2, wherein said compound is Compound 62.

19. The method of claim 2, wherein said compound is Compound 63.

20. The method of claim 2, wherein said compound is Compound 64.

21. The method of claim 2, wherein said compound is Compound 65.

22. The method of claim 2, wherein said compound is Compound 66.

23. The method of claim 2, wherein said compound is Compound 67.

24. The method of claim 2, wherein said compound is Compound 68.

25. The method of claim 2, wherein said compound is Compound 69.

26. The method of claim 2, wherein said compound is Compound 70.

27. The method of claim 2, wherein said compound is Compound 71.

28. The method of claim 2, wherein said compound is Compound 72.

29. The method of claim 2, wherein said compound is Compound 73.

30. The method of claim 2, wherein said compound is Compound 74.

31. The method of claim 2, wherein said compound is Compound 75.

32. The method of claim 2, wherein said compound is Compound 76.

33. The method of claim 2, wherein said compound is Compound 77.

34. The method of claim 2, wherein said compound is Compound 78.

35. The method of claim 2, wherein said compound is Compound 79.

36. The method of claim 2, wherein said compound is Compound 80.

37. The method of claim 2, wherein said compound is Compound 81.

38. The method of claim 2, wherein said compound is Compound 82.

39. The method of claim 2, wherein said compound is Compound 83.

40. The method of claim 2, wherein said compound is Compound 84.

41. The method of claim 2, wherein said compound is Compound 85.

42. The method of claim 2, wherein said compound is Compound 86.

43. The method of claim 2, wherein said compound is Compound 87.

44. The method of claim 2, wherein said compound is Compound 88.

45. The method of claim 2, wherein said compound is Compound 89.

46. The method of claim 2, wherein said compound is Compound 90.

47. The method of claim 2, wherein said compound is Compound 91.

48. The method of claim 2, wherein said compound is Compound 92.

49. The method of claim 2, wherein said compound is Compound 93.

50. The method of claim 2, wherein said compound is Compound 94.

51. The method of claim 2, wherein said compound is Compound 95.

52. The method of claim 2, wherein said compound is Compound 96.

53. The method of claim 2, wherein said compound is Compound 97.

54. The method of claim 2, wherein said compound is Compound 98.

55. The method of claim 2, wherein said compound is Compound 99.

56. The method of claim 2, wherein said compound is Compound 100.

57. The method of claim 2, wherein said compound is Compound 101.

58. The method of claim 2, wherein said compound is Compound 102.

59. The method of claim 2, wherein said compound is Compound 103.

60. The method of claim 2, wherein said compound is Compound 104.

61. The method of claim 2, wherein said compound is Compound 105.

62. The method of claim 2, wherein said compound is Compound 106.

63. The method of claim 2, wherein said compound is Compound 107.

64. The method of claim 2, wherein said compound is Compound 108.

65. The method of claim 2, wherein said compound is Compound 109.

66. The method of claim 2, wherein said compound is Compound 110.

67. The method of claim 2, wherein said compound is Compound 111.

68. The method of claim 2, wherein said compound is Compound 112.

69. The method of claim 2, wherein said compound is Compound 113.

70. The method of claim 2, wherein said compound is Compound 114.

71. The method of claim 2, wherein said compound is Compound 115.

72. The method of claim 2, wherein said compound is Compound 116.

73. The method of claim 2, wherein said compound is Compound 117.

74. The method of claim 2, wherein said compound is Compound 118.

75. The method of claim 2, wherein said compound is Compound 119.

76. The method of claim 2, wherein said compound is Compound 120.

77. The method of claim 2, wherein said compound is Compound 121.

78. The method of claim 2, wherein said compound is Compound 122.

79. The method of claim 2, wherein said compound is Compound 123.

80. The method of claim 2, wherein said compound is Compound 124.

81. The method of claim 2, wherein said compound is Compound 125.

82. The method of claim 2, wherein said compound is Compound 126.

83. The method of claim 2, wherein said compound is Compound 127.

84. The method of claim 2, wherein said compound is Compound 128.

85. The method of claim 2, wherein said compound is Compound 129.

86. The method of claim 2, wherein said compound is Compound 130.

87. The method of claim 2, wherein said compound is Compound 131.

88. The method of claim 2, wherein said compound is Compound 132.

89. The method of claim 2, wherein said compound is Compound 133.

90. The method of claim 2, wherein said compound is Compound 134.

91. The method of claim 2, wherein said compound is Compound 135.

92. The method of claim 2, wherein said compound is Compound 136.

93. The method of claim 2, wherein said compound is Compound 137.

94. The method of claim 2, wherein said compound is Compound 138.

95. The method of claim 2, wherein said compound is Compound 139.

96. The method of claim 2, wherein said compound is Compound 140.

97. The method of claim 2, wherein said compound is Compound 141.

98. The method of claim 2, wherein said compound is Compound 142.

99. The method of claim 2, wherein said compound is Compound 143.

100. The method of claim 2, wherein said compound is Compound 144.

101. The method of claim 2, wherein said compound is Compound 145.

102. The method of claim 2, wherein said compound is Compound 146.

103. The method of claim 2, wherein said compound is Compound 147.

104. The method of claim 2, wherein said compound is Compound 148.

105. The method of claim 2, wherein said compound is Compound 149.

106. The method of claim 2, wherein said compound is Compound 150.

107. The method of claim 2, wherein said compound is Compound 151.

108. The method of claim 2, wherein said compound is Compound 152.

109. The method of claim 2, wherein said compound is Compound 153.

110. The method of claim 2, wherein said compound is Compound 154.

111. The method of claim 2, wherein said compound is Compound 155.

112. The method of claim 2, wherein said compound is Compound 156.

113. The method of claim 2, wherein said compound is Compound 157.

114. The method of claim 2, wherein said compound is Compound 158.

115. The method of claim 2, wherein said compound is Compound 159.

116. The method of claim 2, wherein said compound is Compound 160.

117. The method of claim 2, wherein said compound is Compound 161.

118. The method of claim 2, wherein said compound is Compound 162.

119. The method of claim 2, wherein said compound is Compound 163.

120. The method of claim 2, wherein said compound is Compound 164.

121. The method of claim 2, wherein said compound is Compound 165.

122. The method of claim 2, wherein said compound is Compound 166.

123. The method of claim 2, wherein said compound is Compound 167.

124. The method of claim 2, wherein said compound is Compound 168.

125. The method of claim 2, wherein said compound is Compound 169.

126. The method of claim 2, wherein said compound is Compound 170.

127. The method of claim 2, wherein said compound is Compound 171.

128. The method of claim 2, wherein said compound is Compound 172.

129. The method of claim 2, wherein said compound is Compound 173.

130. The method of claim 2, wherein said compound is Compound 174.

131. The method of claim 2, wherein said compound is Compound 175.

132. The method of claim 2, wherein said compound is Compound 176.

133. The method of claim 2, wherein said compound is Compound 177.

134. The method of claim 2, wherein said compound is Compound 178.

135. The method of claim 2, wherein said compound is Compound 179.

136. The method of claim 2, wherein said compound is Compound 180.

137. The method of claim 2, wherein said compound is Compound 181.

138. The method of claim 2, wherein said compound is Compound 182.

139. The method of claim 2, wherein said compound is Compound 183.

140. The method of claim 2, wherein said compound is Compound 184.

141. The method of claim 2, wherein said compound is Compound 185.

142. The method of claim 2, wherein said compound is Compound 186.

143. The method of claim 2, wherein said compound is Compound 187.

144. The method of claim 2, wherein said compound is Compound 188.

145. The method of claim 2, wherein said compound is Compound 189.

146. The method of claim 2, wherein said compound is Compound 190.

147. The method of claim 2, wherein said compound is Compound 191.

148. The method of claim 2, wherein said compound is Compound 192.

149. The method of claim 2, wherein said compound is Compound 193.

150. The method of claim 2, wherein said compound is Compound 194.

151. The method of claim 2, wherein said compound is Compound 195.

152. The method of claim 2, wherein said compound is Compound 196.

153. The method of claim 2, wherein said compound is Compound 197.

154. The method of claim 2, wherein said compound is Compound 198.

155. The method of claim 2, wherein said compound is Compound 199.

156. The method of claim 2, wherein said compound is Compound 200.

157. The method of claim 2, wherein said compound is Compound 201.

158. The method of claim 2, wherein said compound is Compound 202.

159. The method of claim 2, wherein said compound is Compound 203.

160. The method of claim 2, wherein said compound is Compound 204.

161. The method of claim 2, wherein said compound is Compound 205.

162. The method of claim 2, wherein said compound is Compound 206.

163. The method of claim 2, wherein said compound is Compound 207.

164. The method of claim 2, wherein said compound is Compound 208.

165. The method of claim 2, wherein said compound is Compound 209.

166. The method of claim 2, wherein said compound is Compound 210.

167. The method of claim 2, wherein said compound is Compound 211.

168. The method of claim 2, wherein said compound is Compound 212.

169. The method of claim 2, wherein said compound is Compound 213.

170. The method of claim 2, wherein said compound is Compound 214.

171. The method of claim 2, wherein said compound is Compound 215.

172. The method of claim 2, wherein said compound is Compound 216.

173. The method of claim 2, wherein said compound is Compound 217.

174. The method of claim 2, wherein said compound is Compound 218.

175. The method of claim 2, wherein said compound is Compound 219.

176. The method of claim 2, wherein said compound is Compound 220.

177. The method of claim 2, wherein said compound is Compound 221.

178. The method of claim 2, wherein said compound is Compound 222.

179. The method of claim 2, wherein said compound is Compound 223.

180. The method of claim 2, wherein said compound is Compound 224.

181. The method of claim 2, wherein said compound is Compound 225.

182. The method of claim 2, wherein said compound is Compound 226.

FIG. 1

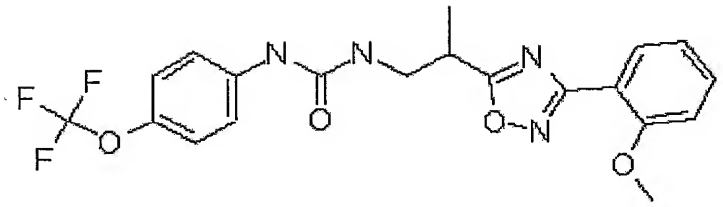


FIG. 2

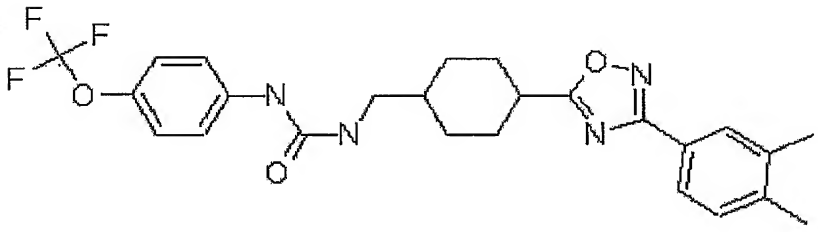


FIG. 3

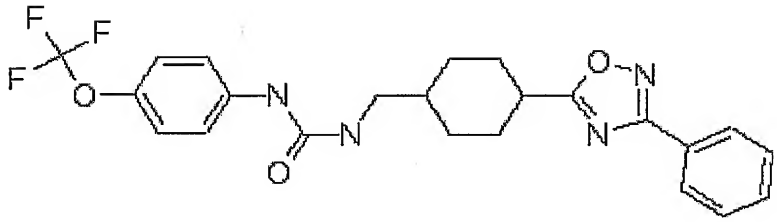


FIG. 4

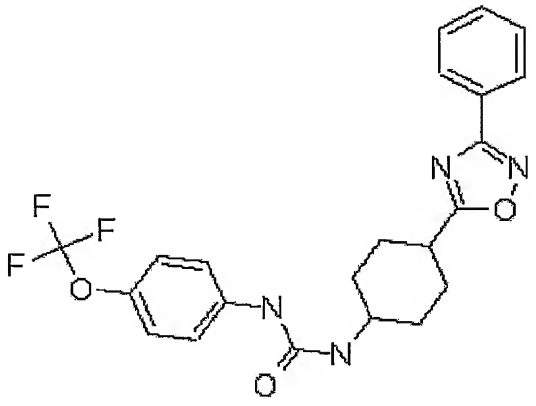


FIG. 5

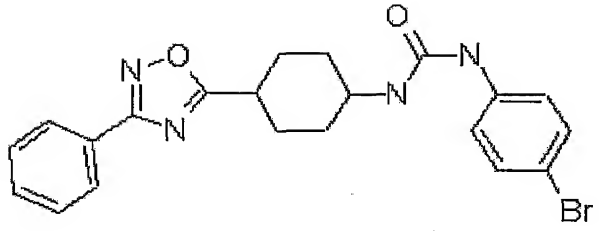


FIG. 6

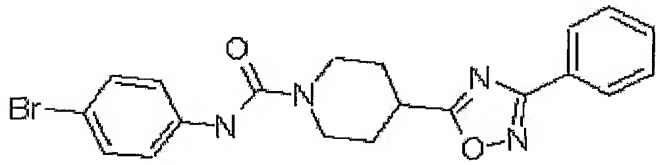


FIG. 7

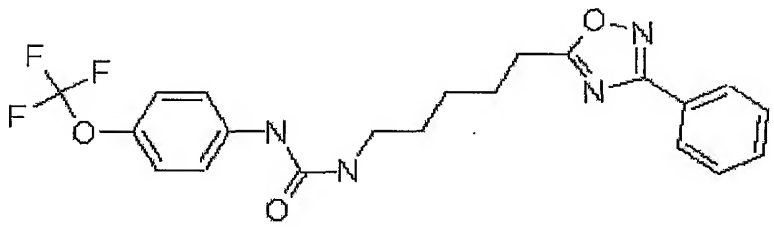


FIG. 8

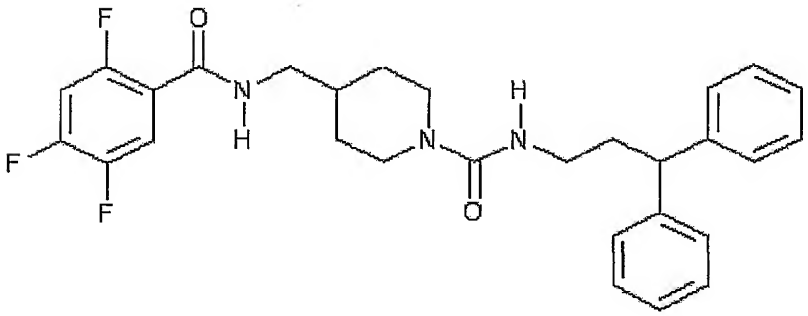


FIG. 9

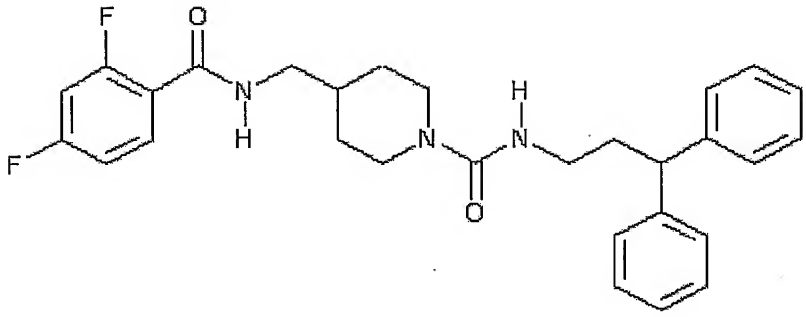


FIG. 10

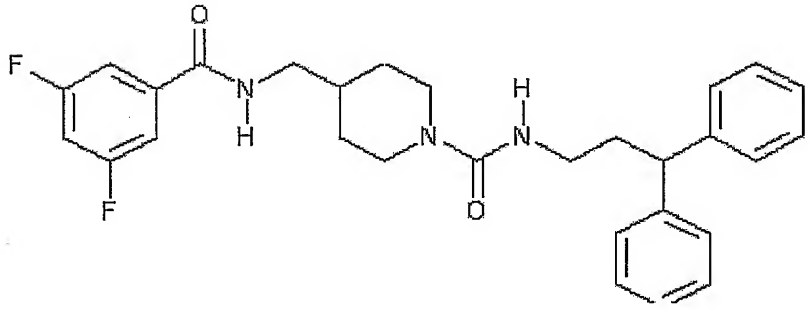


FIG. 11

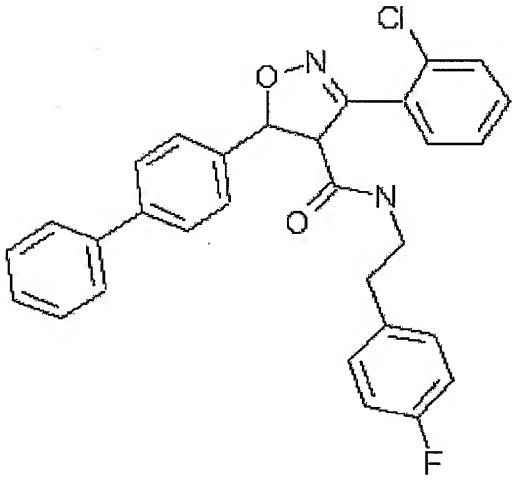


FIG. 12

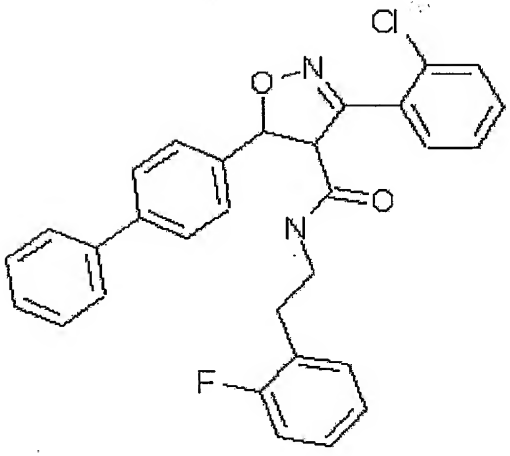


FIG. 13

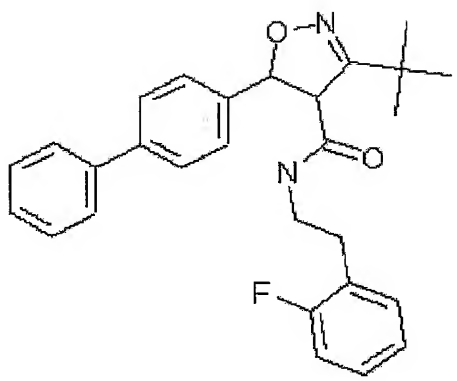


FIG. 14

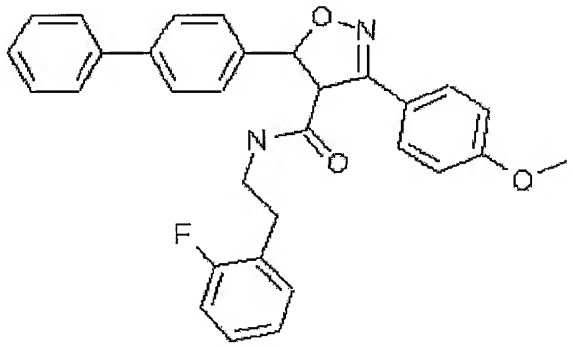


FIG. 15

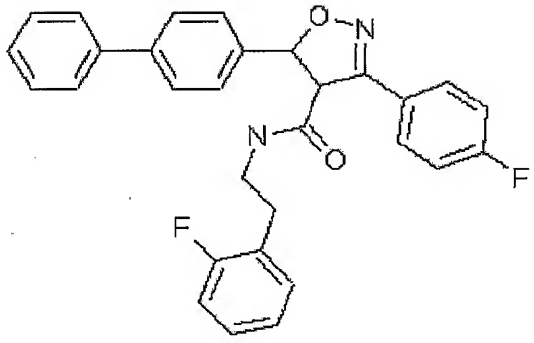


FIG. 16

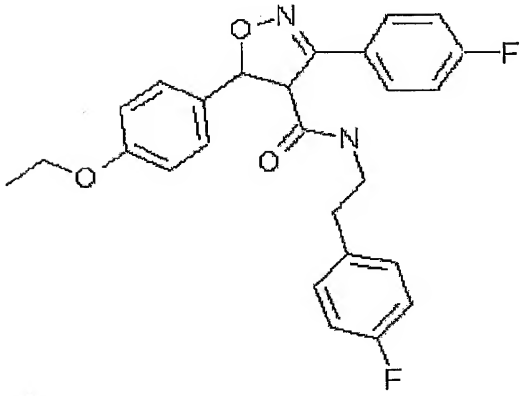


FIG. 17

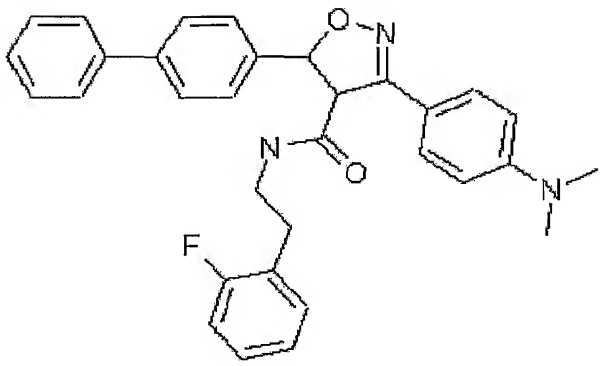


FIG. 18

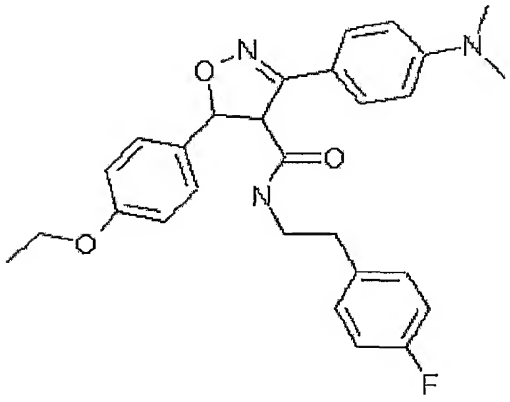


FIG. 19

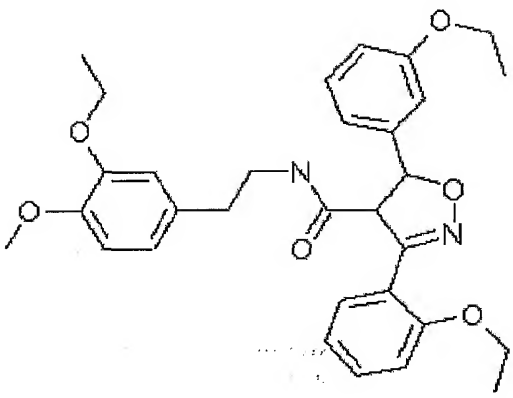


FIG. 20

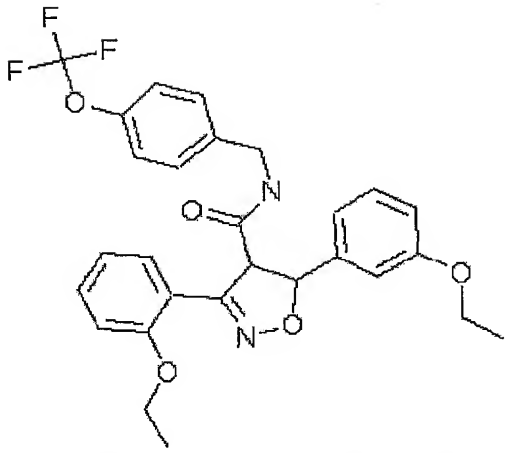


FIG. 21

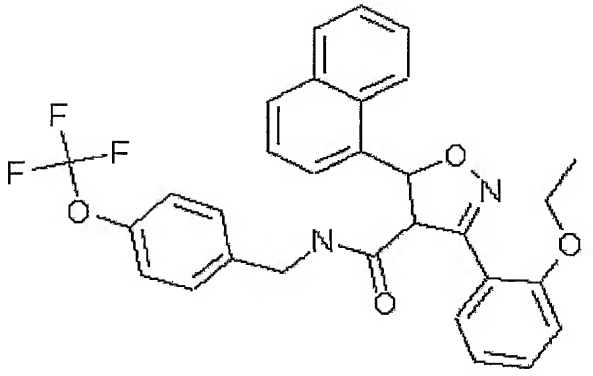


FIG. 22

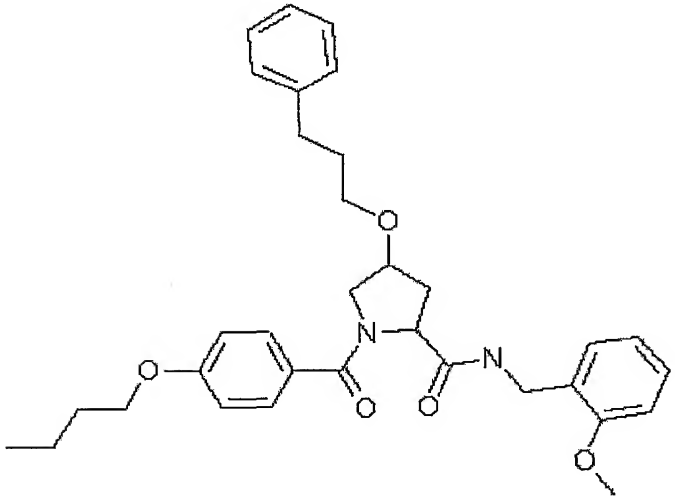


FIG. 23

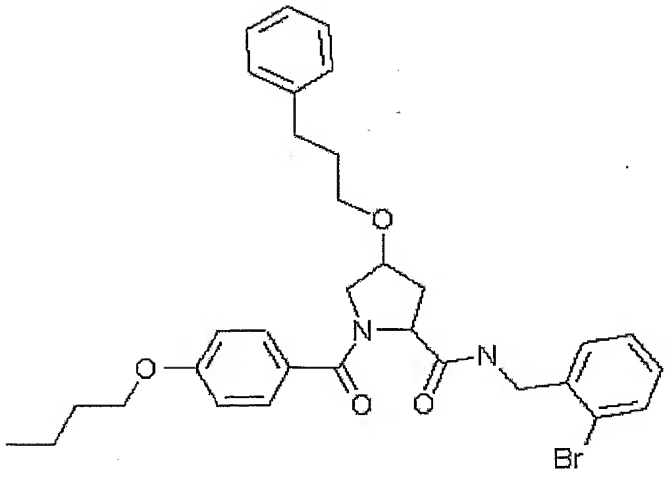


FIG. 24

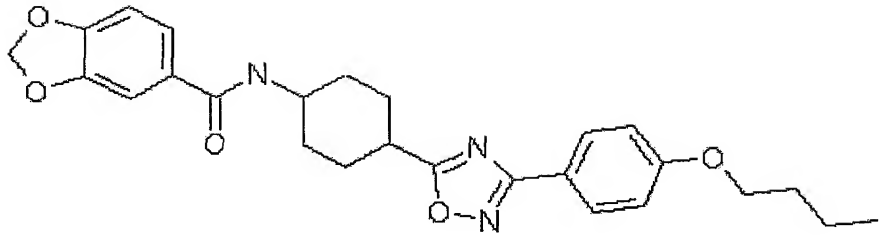


FIG. 25

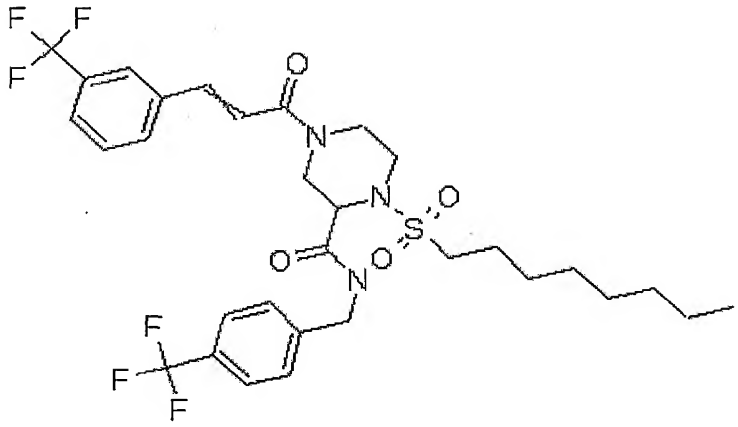


FIG. 26

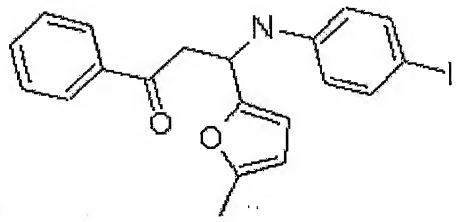


FIG. 27

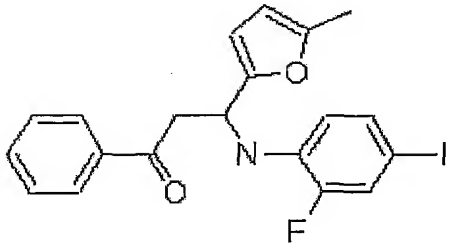


FIG. 28

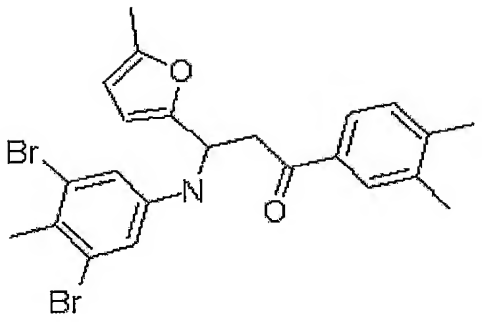


FIG. 29

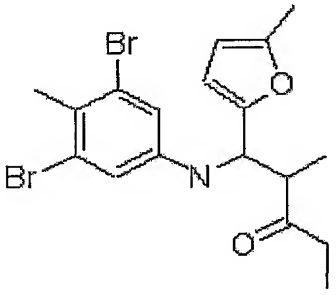


FIG. 30

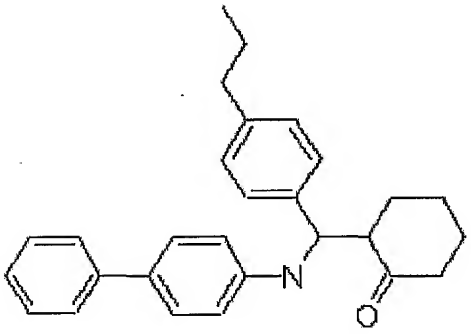


FIG. 31

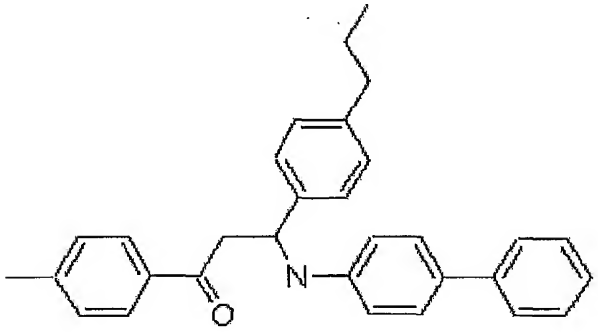


FIG. 32

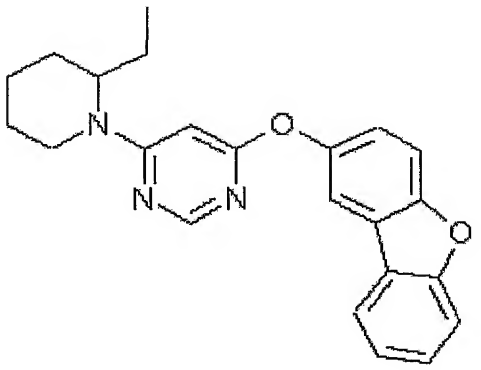


FIG. 33

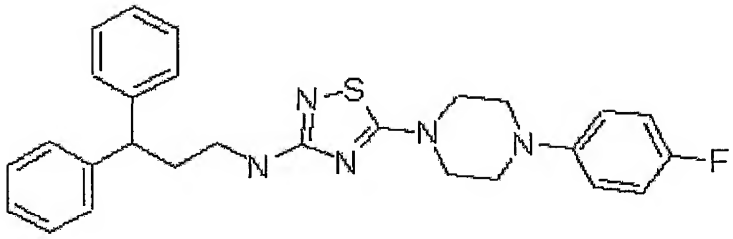


FIG. 34

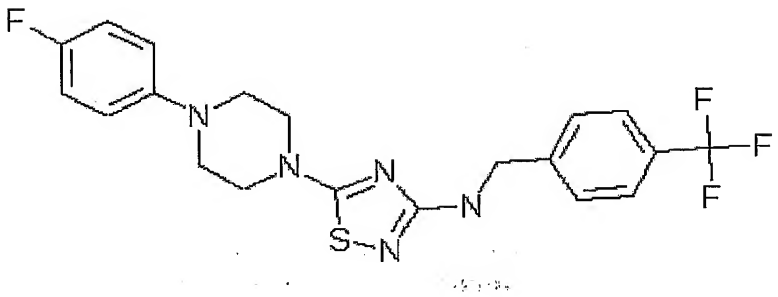


FIG. 35

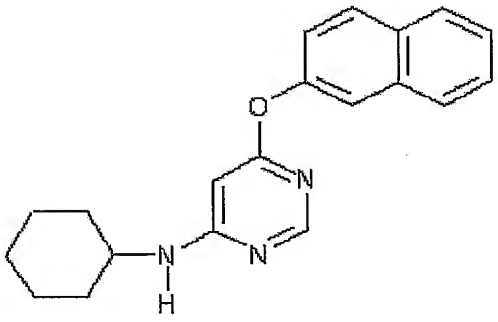


FIG. 36

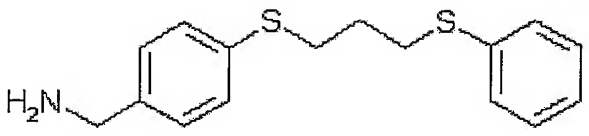


FIG. 37

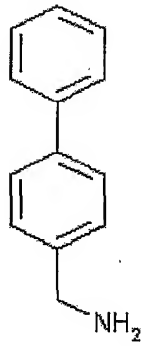


FIG. 38

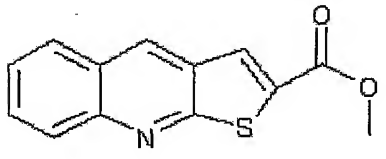


FIG. 39

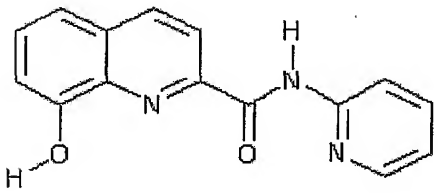


FIG. 40

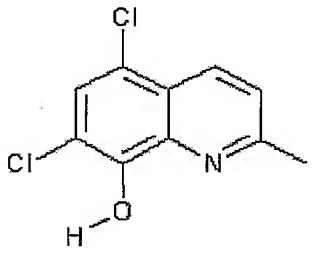


FIG. 41

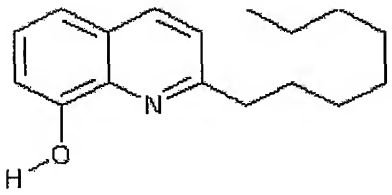


FIG. 42

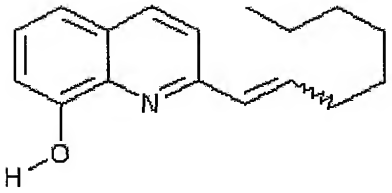


FIG. 43

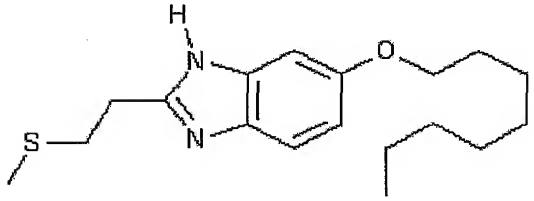


FIG. 44

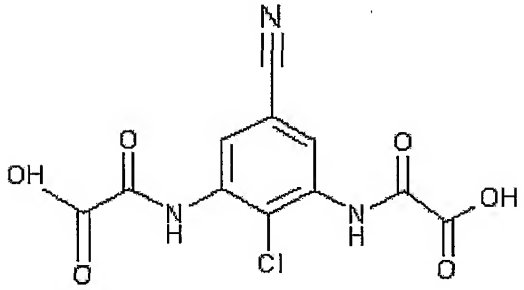


FIG. 45

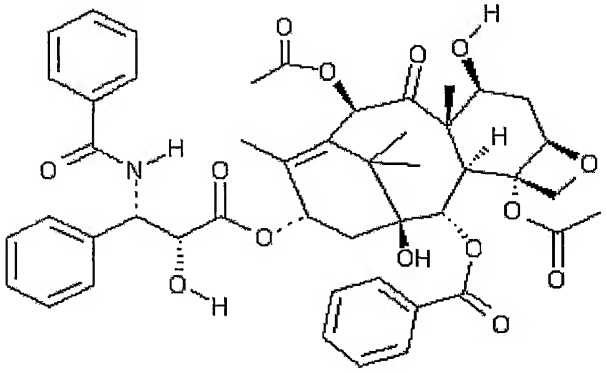


FIG. 46

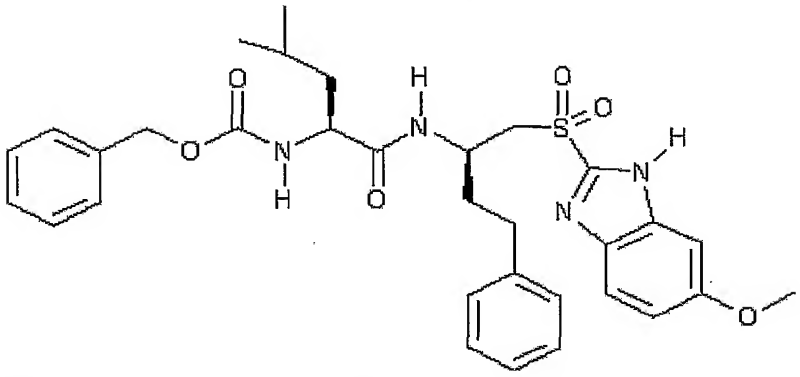


FIG. 47

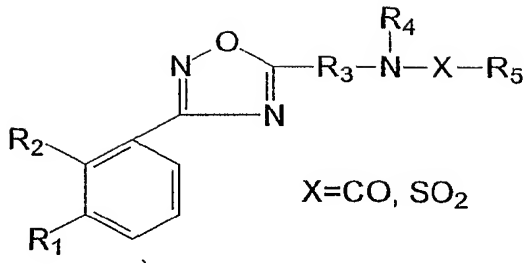


FIG. 48

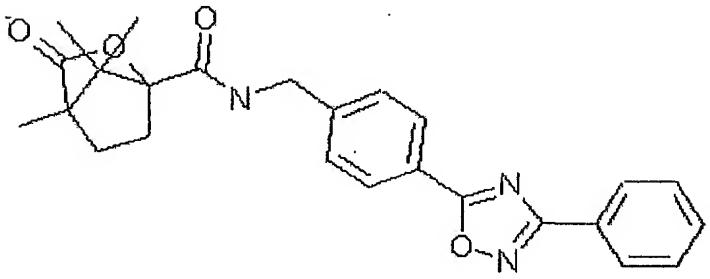


FIG. 49

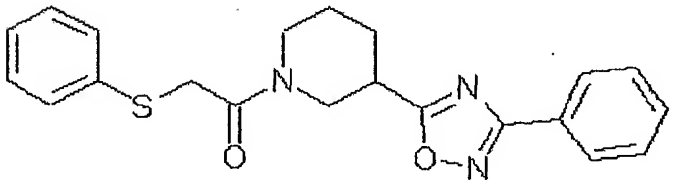


FIG. 50

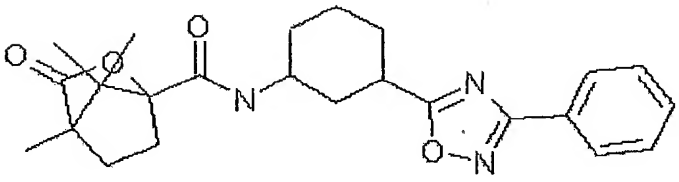


FIG. 51

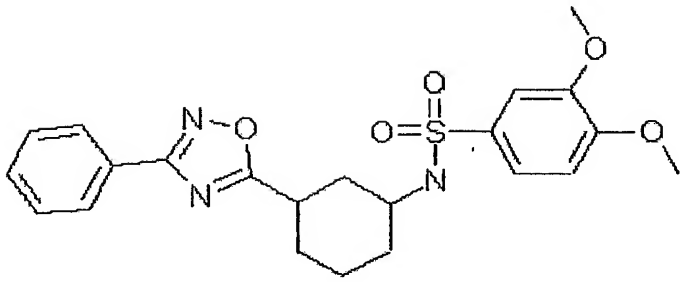


FIG. 52

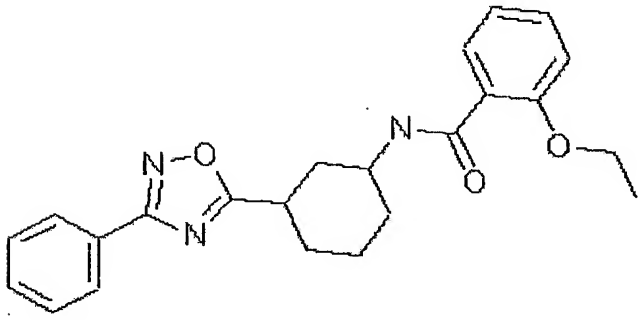


FIG. 53

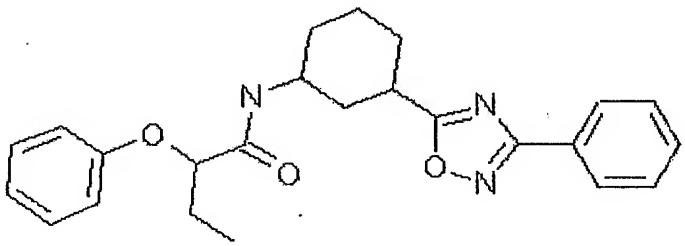


FIG. 54

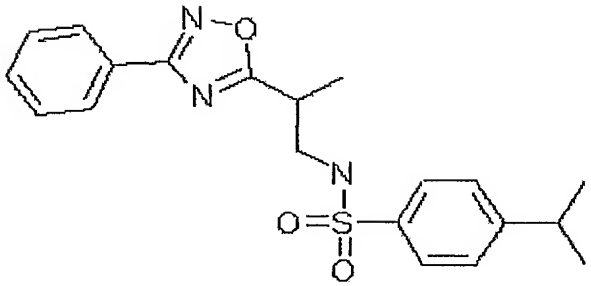


FIG. 55

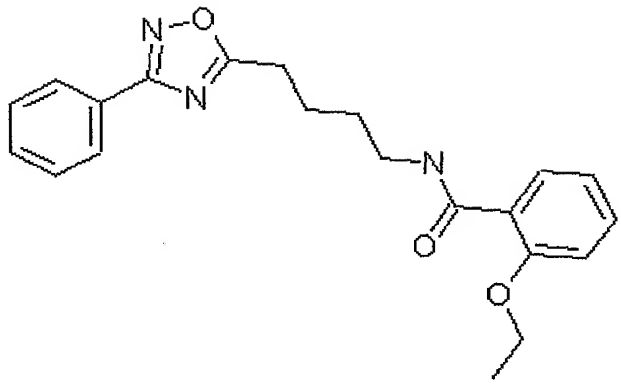


FIG. 56

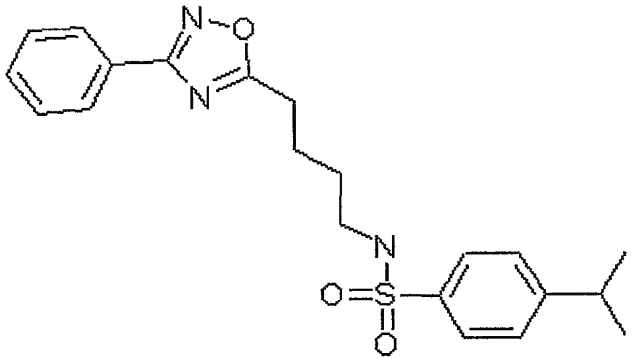


FIG. 57

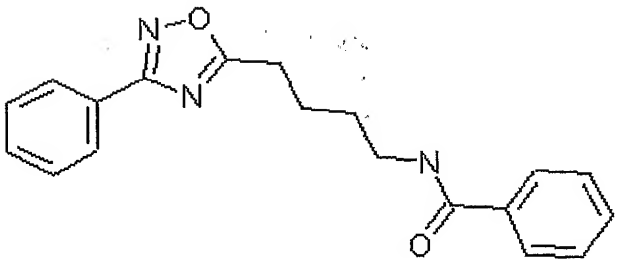


FIG. 58

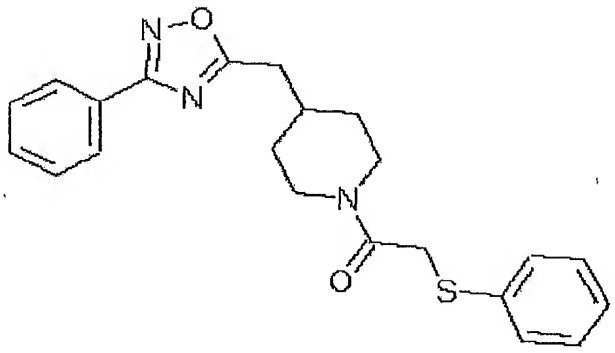


FIG. 59

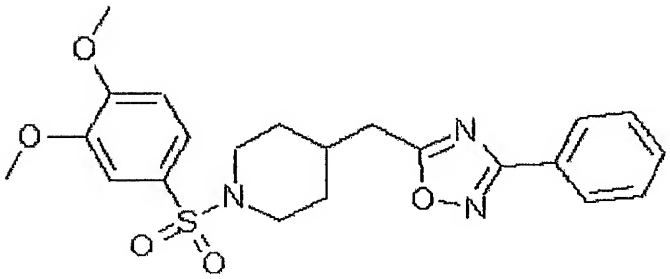


FIG. 60

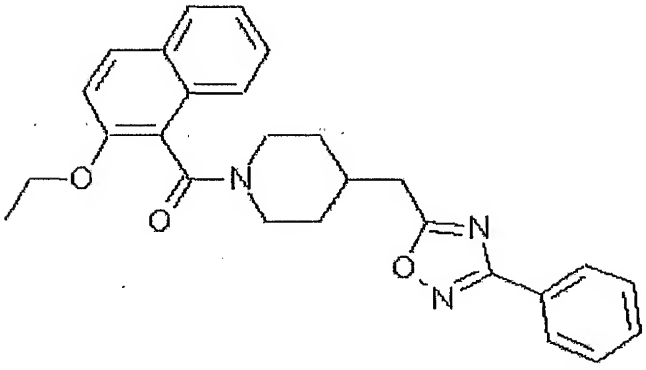


FIG. 61

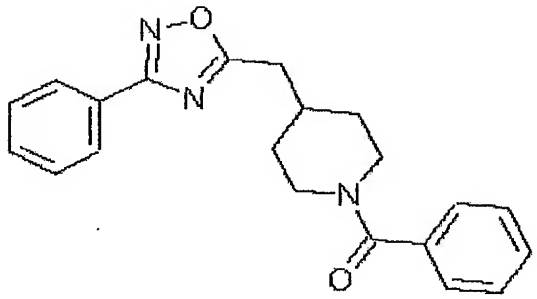


FIG. 62

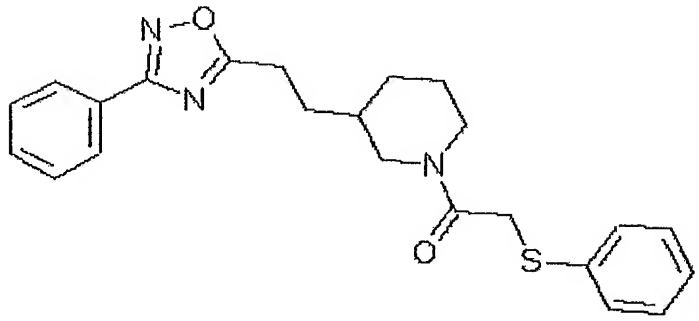


FIG. 63

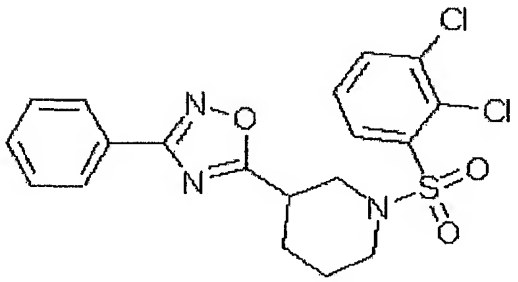


FIG. 64

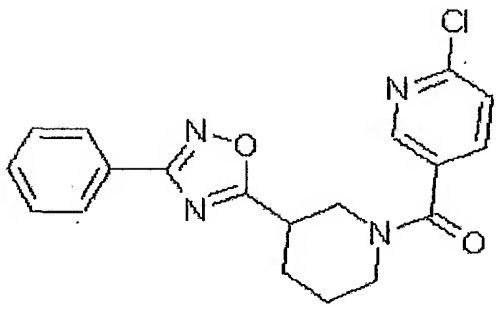


FIG. 65

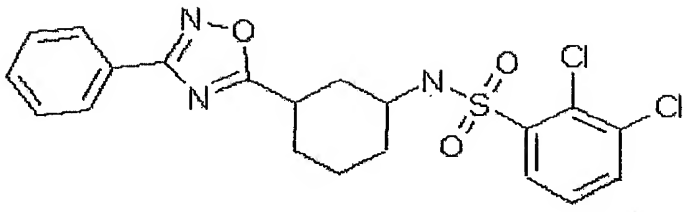


FIG. 66

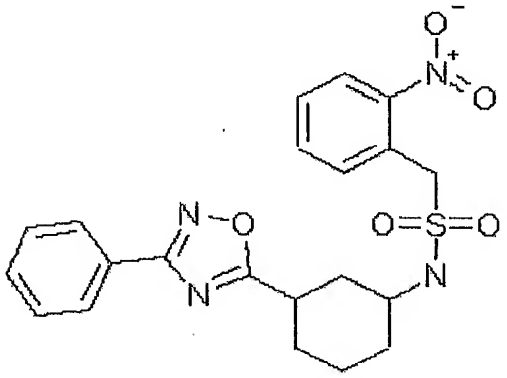


FIG. 67

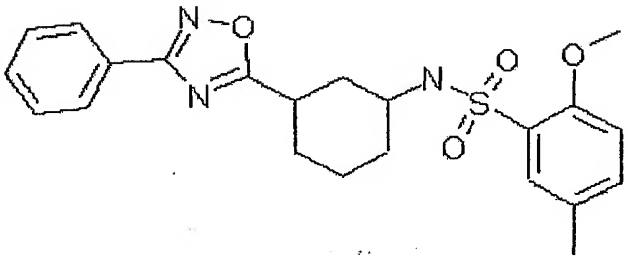


FIG. 68

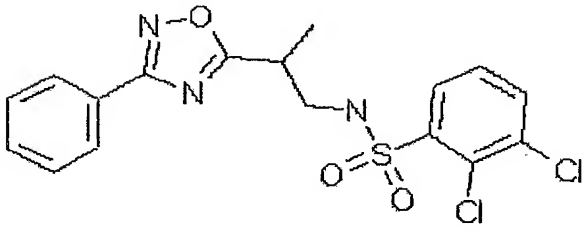


FIG. 69

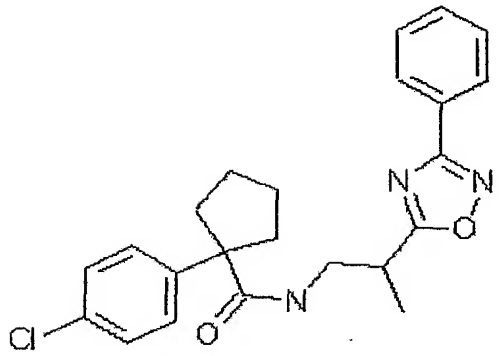


FIG. 70

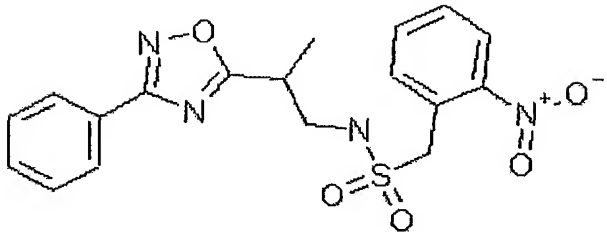


FIG. 71

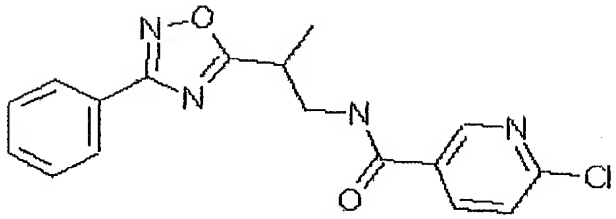


FIG. 72

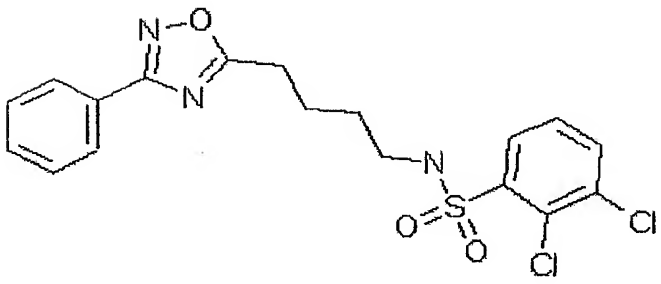


FIG. 73

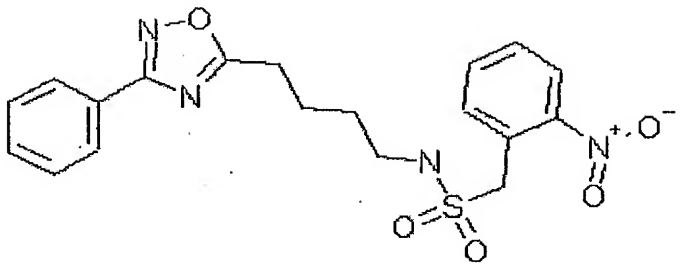


FIG. 74

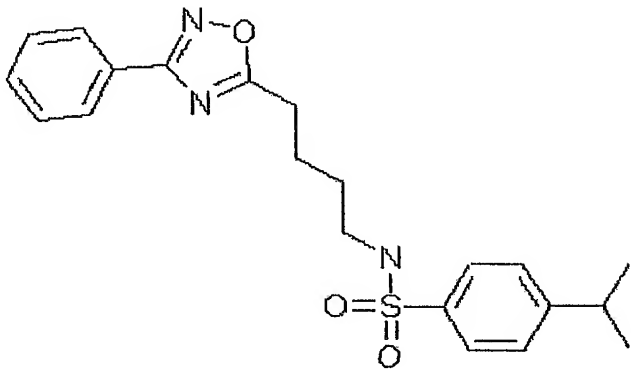


FIG. 75

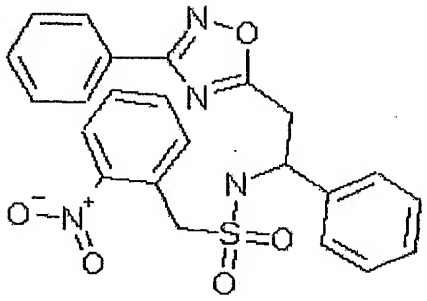


FIG. 76

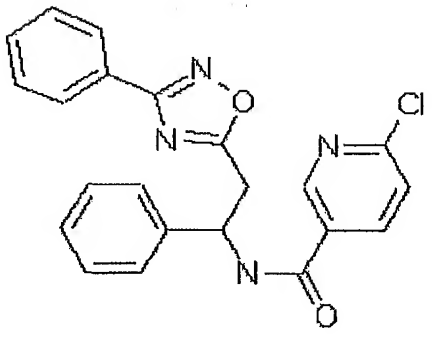


FIG. 77

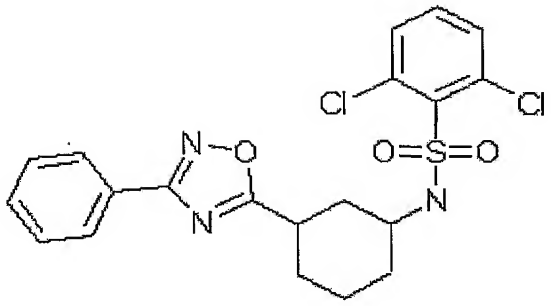


FIG. 78

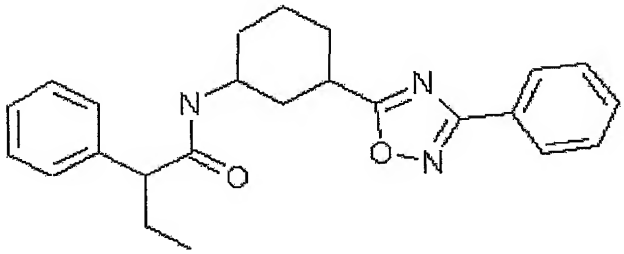


FIG. 79

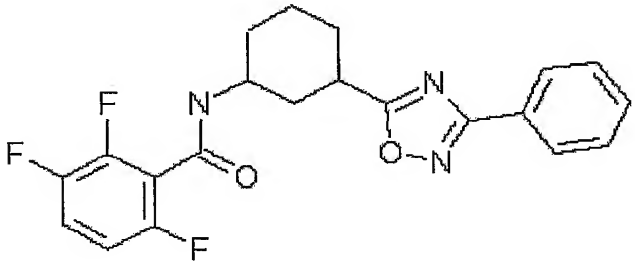


FIG. 80

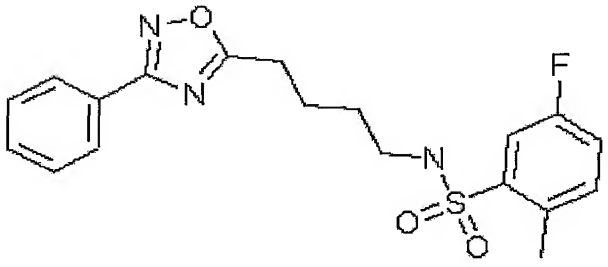


FIG. 81

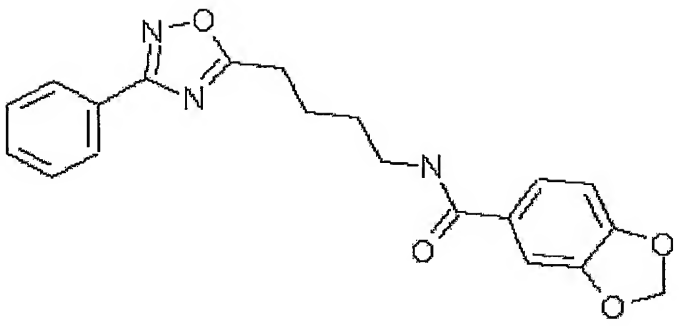


FIG. 82

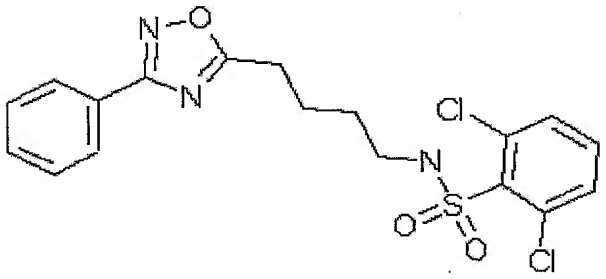


FIG. 83

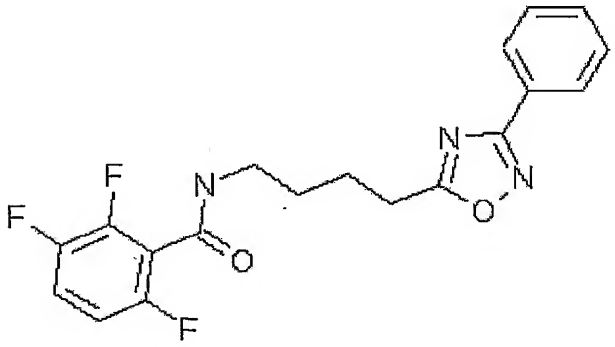


FIG. 84

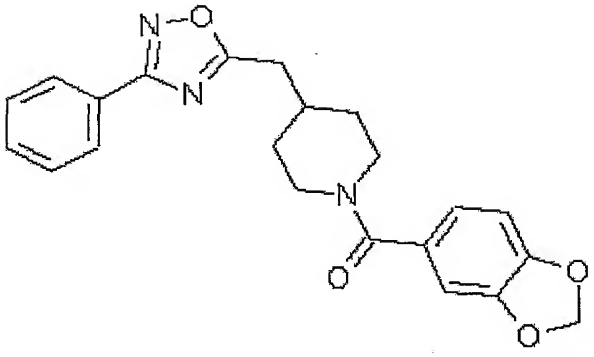


FIG. 85

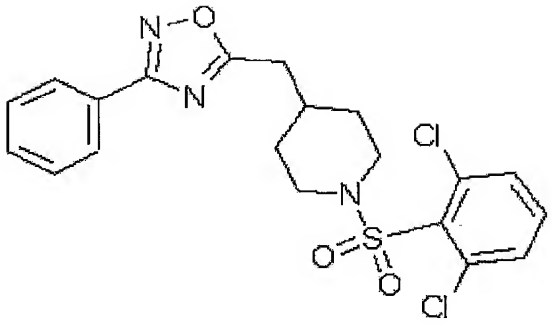


FIG. 86

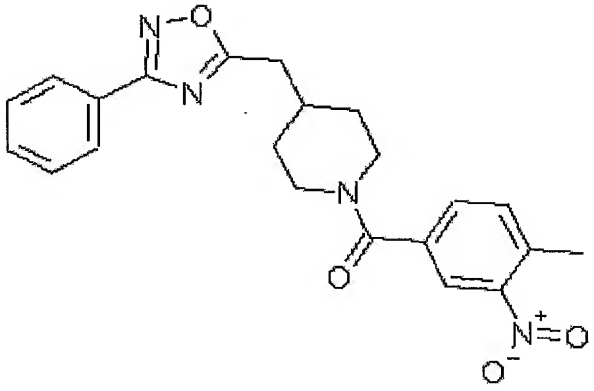


FIG. 87

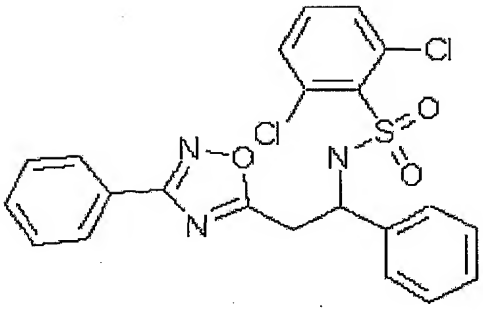


FIG. 88

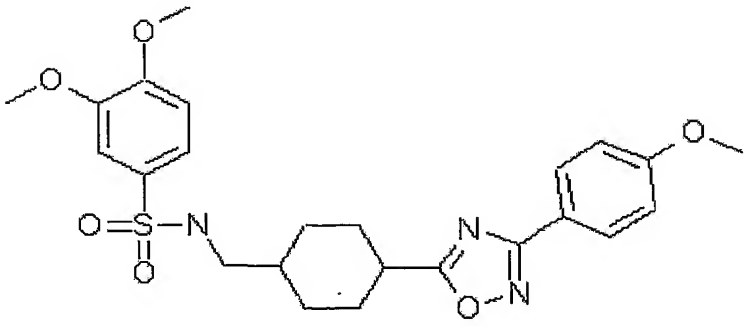


FIG. 89

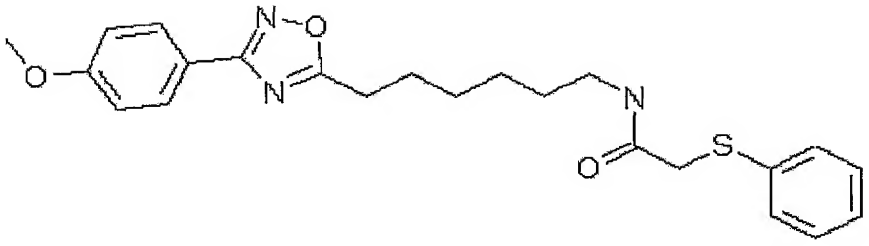


FIG. 90

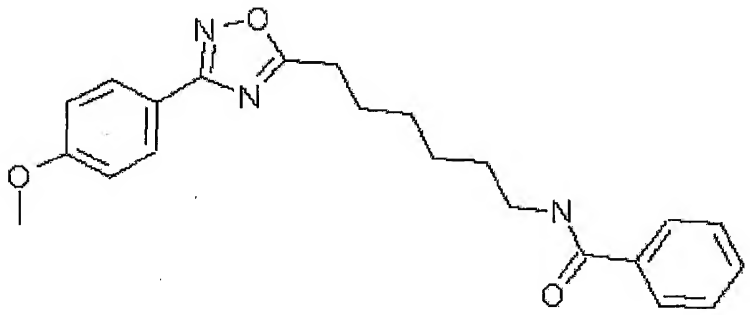


FIG. 91

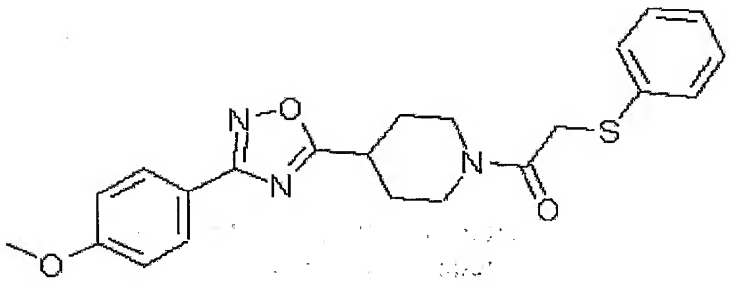


FIG. 92

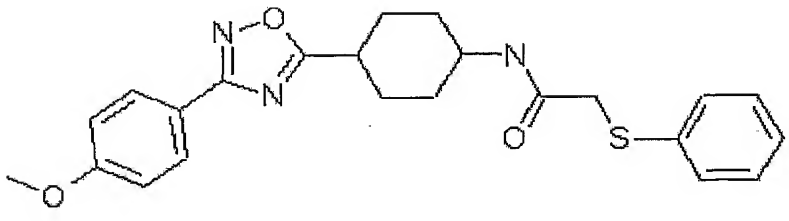


FIG. 93

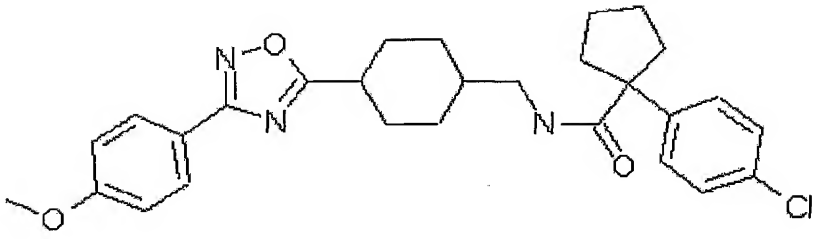


FIG. 94

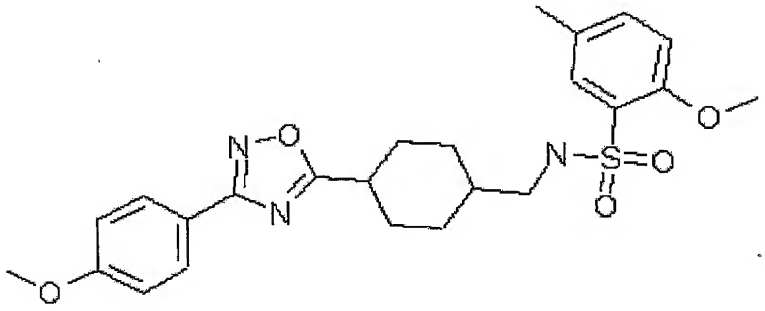


FIG. 95

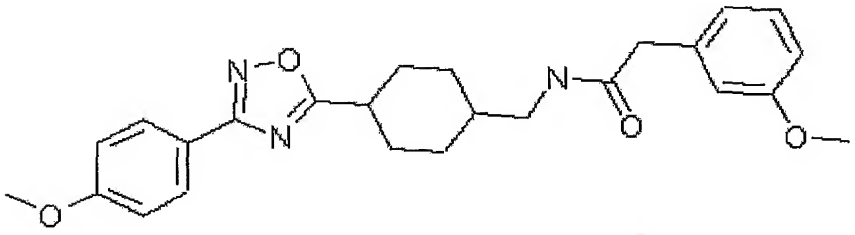


FIG. 96

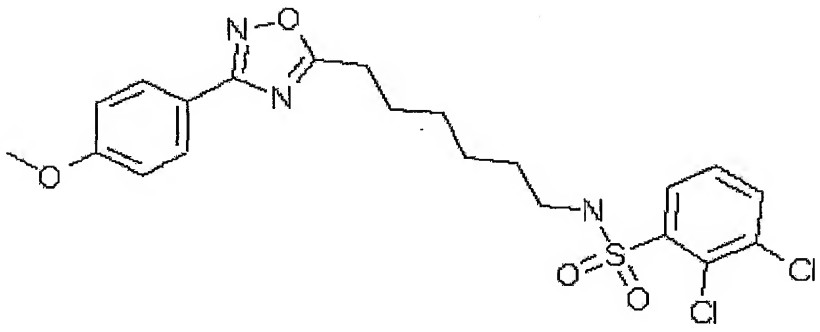


FIG. 97

FIG. 98

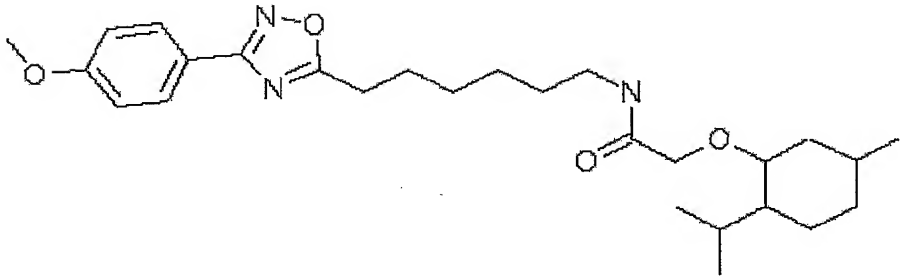


FIG. 99

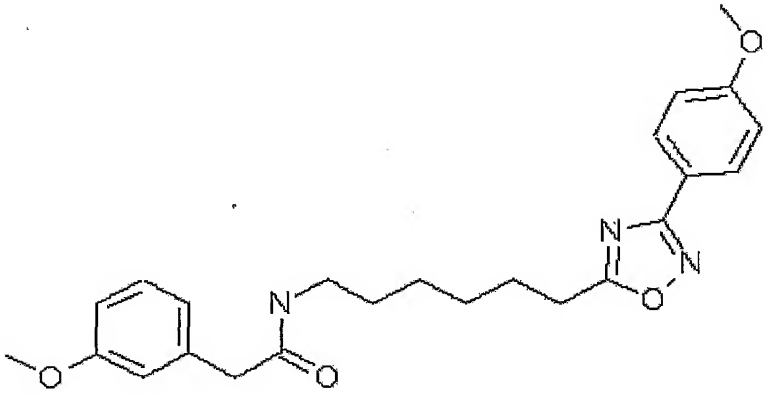


FIG. 100

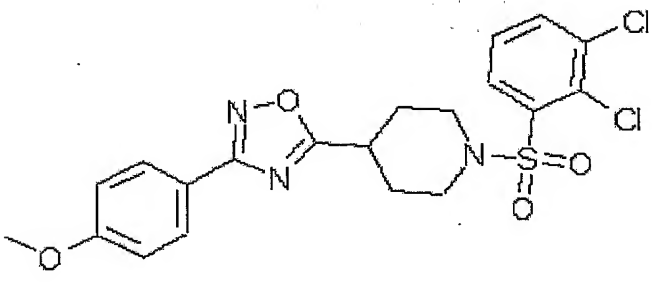


FIG. 101

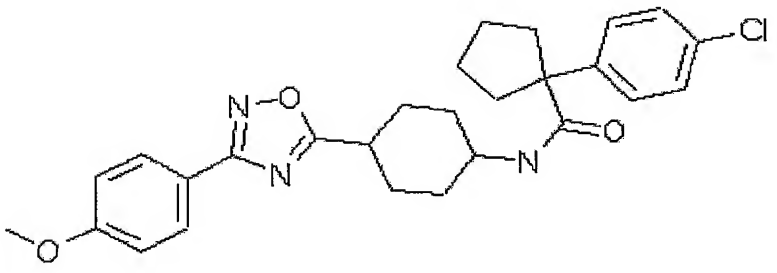


FIG. 102

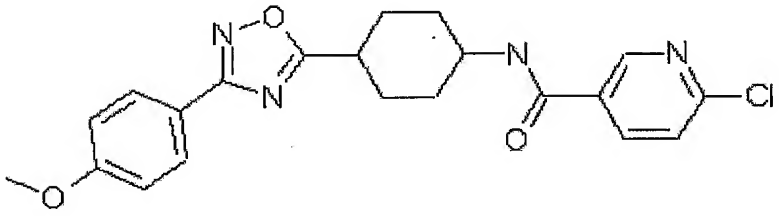


FIG. 103

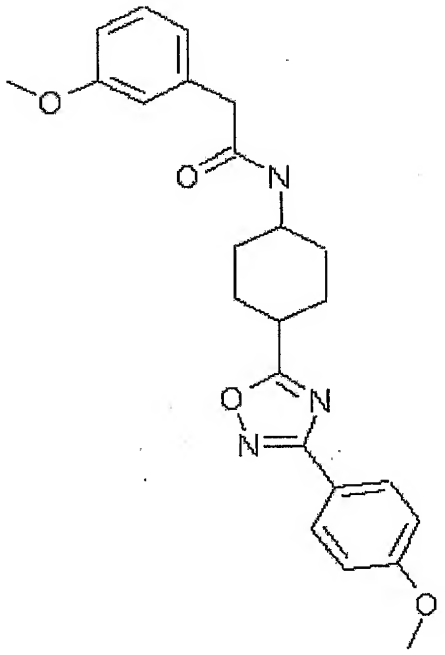


FIG. 104

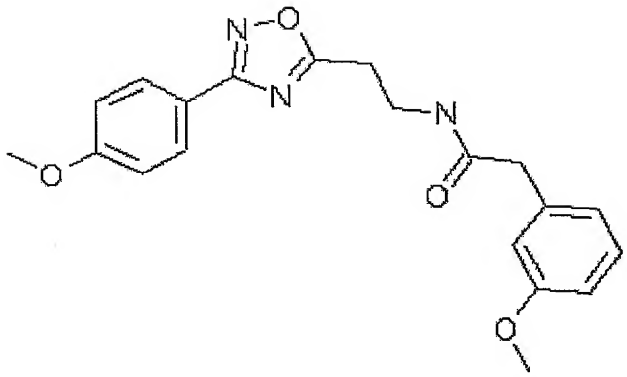


FIG. 105

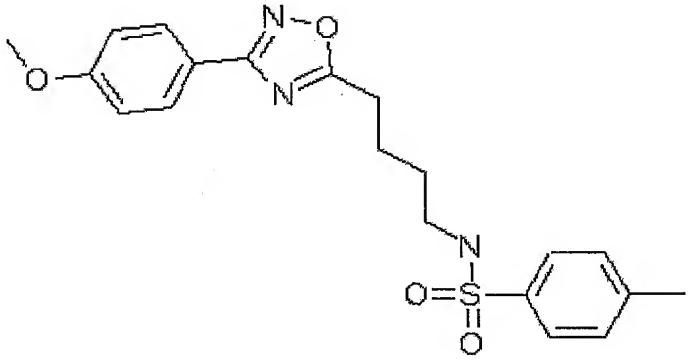


FIG. 106

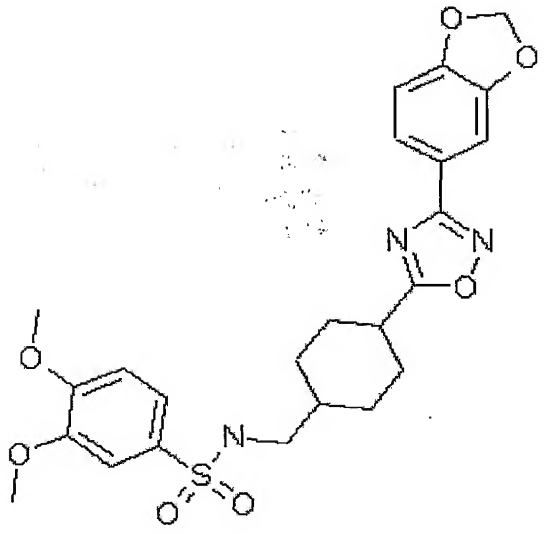


FIG. 107

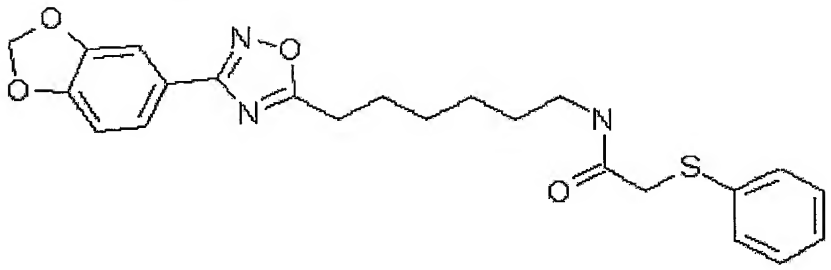


FIG. 108

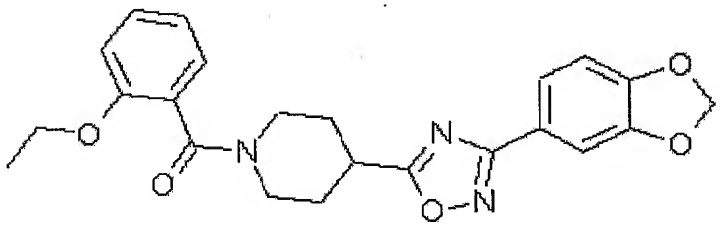


FIG. 109

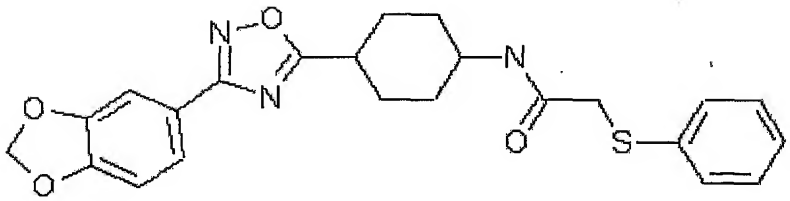


FIG. 110

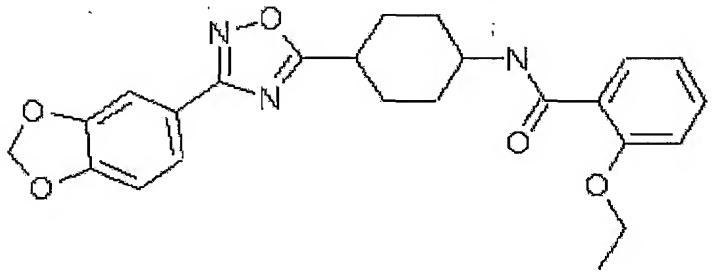


FIG. 111

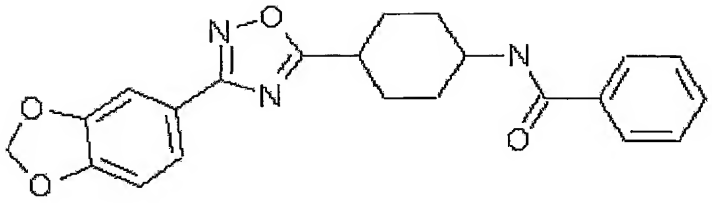


FIG. 112

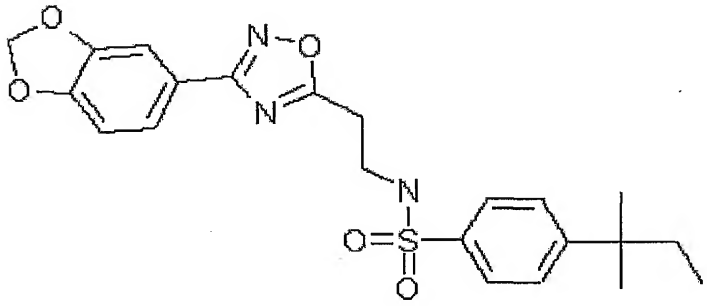


FIG. 113

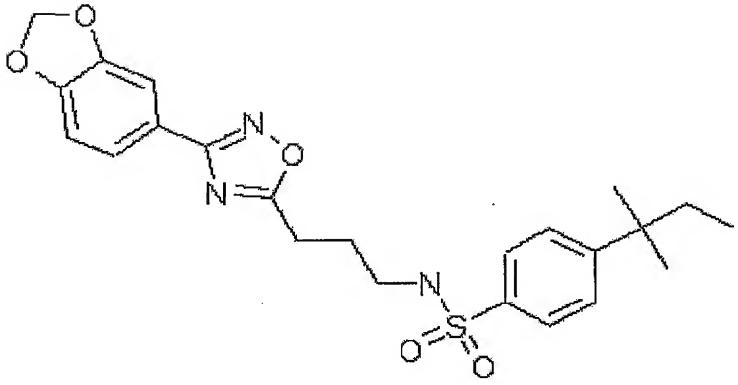


FIG. 114

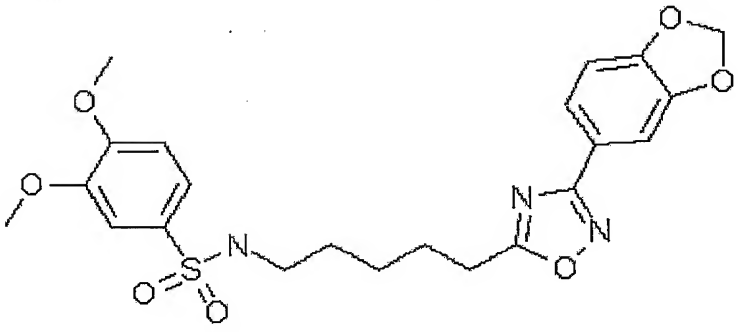


FIG. 115

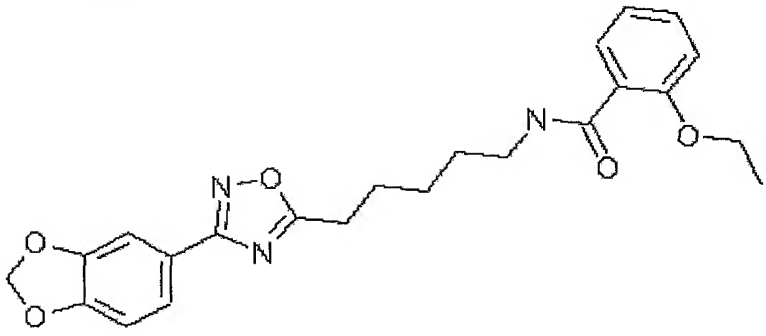


FIG. 116

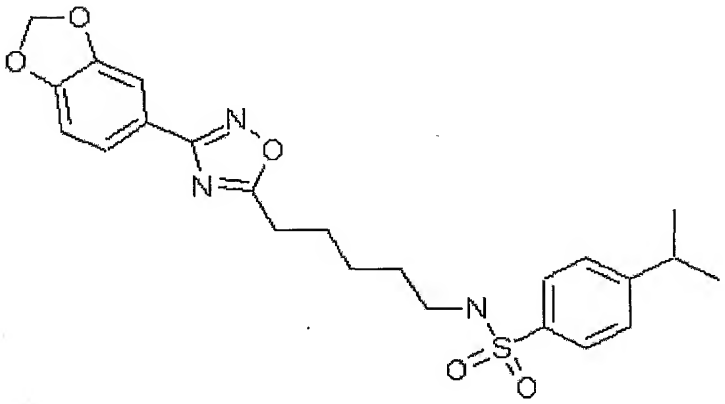


FIG. 117

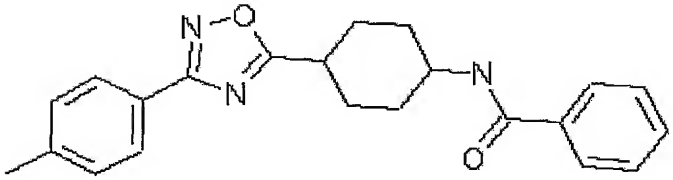


FIG. 118

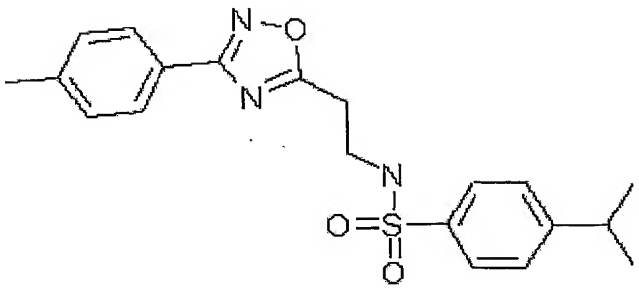


FIG. 119

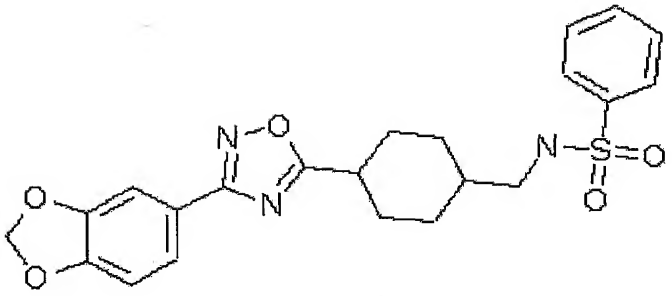


FIG. 120

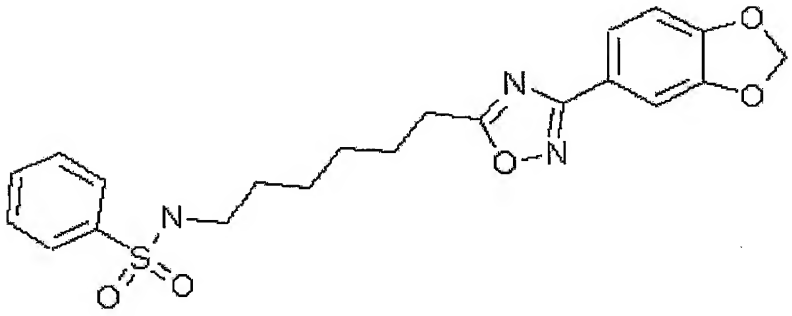


FIG. 121

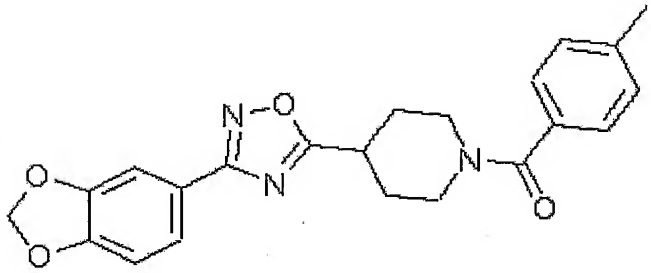


FIG. 122

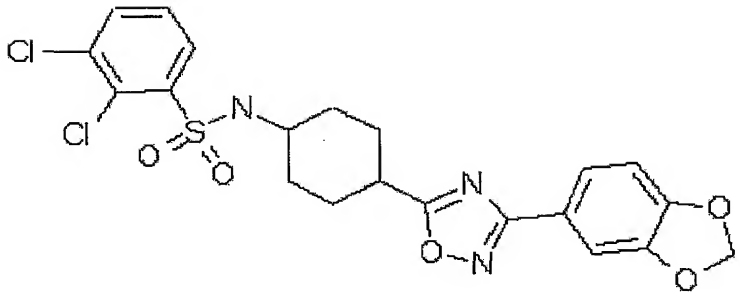


FIG. 123

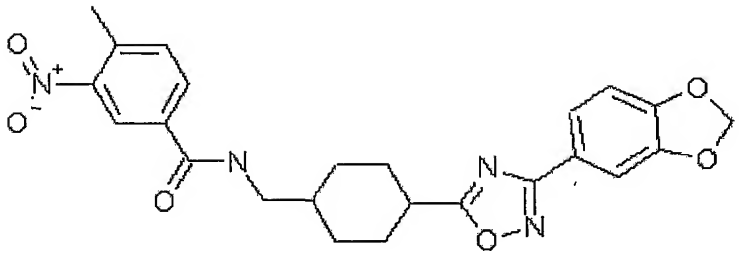


FIG. 124

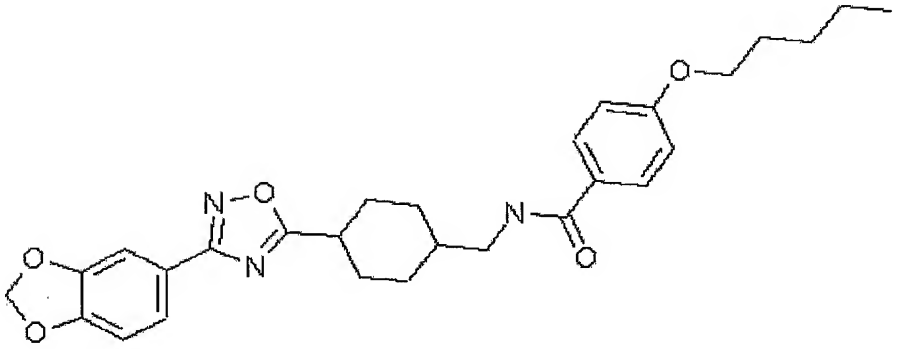


FIG. 125

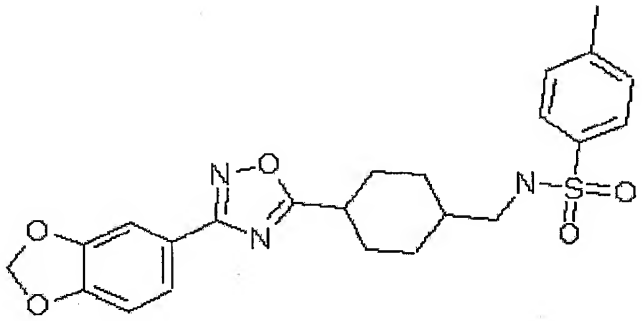


FIG. 126

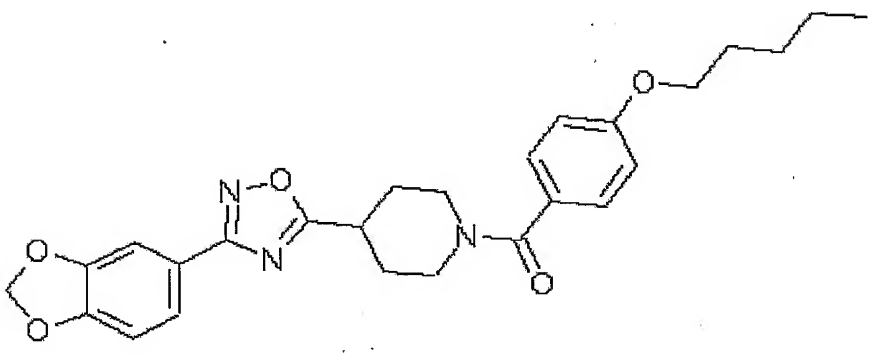


FIG. 127

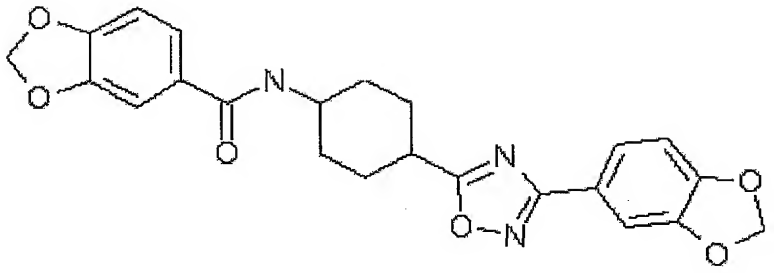


FIG. 128

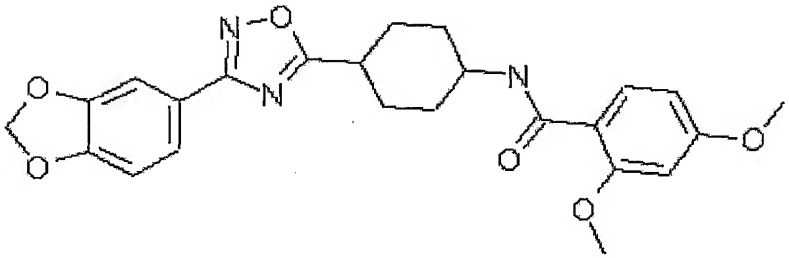


FIG. 129

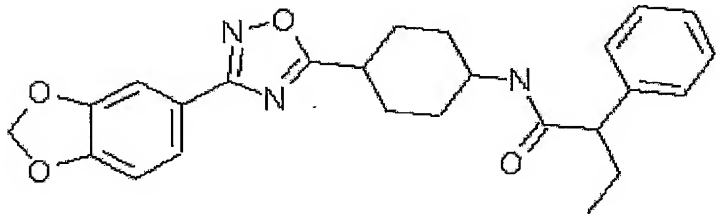


FIG. 130

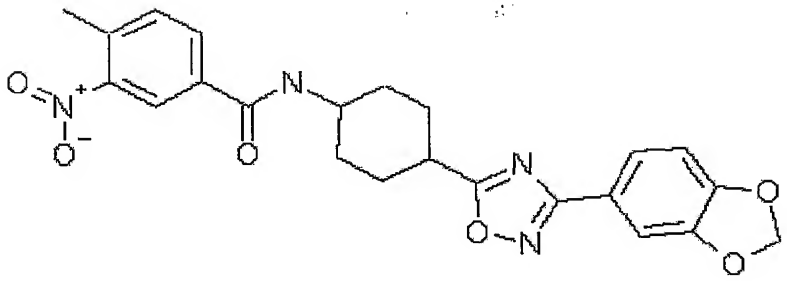


FIG. 131

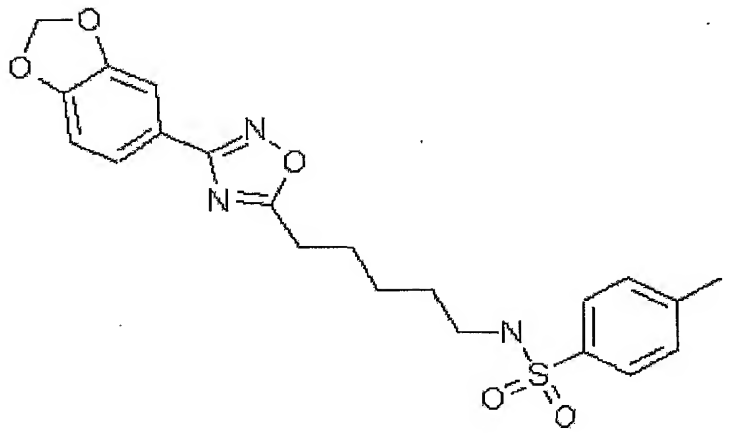


FIG. 132

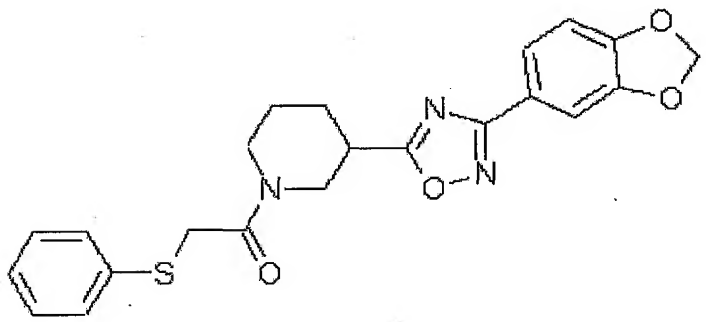


FIG. 133

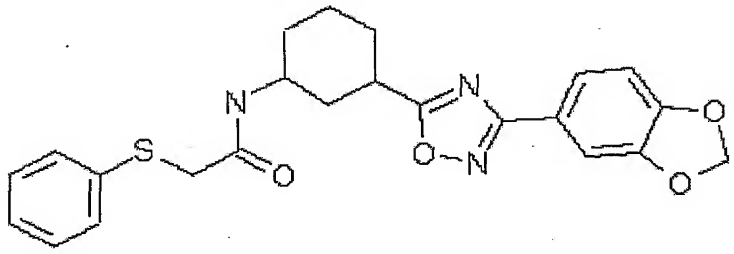


FIG. 134

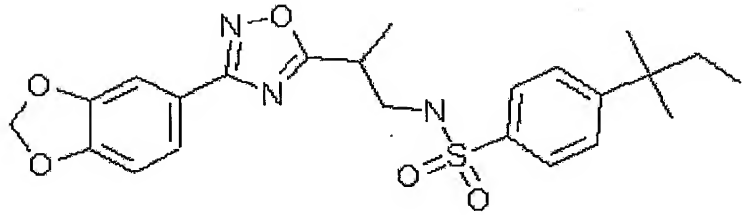


FIG. 135

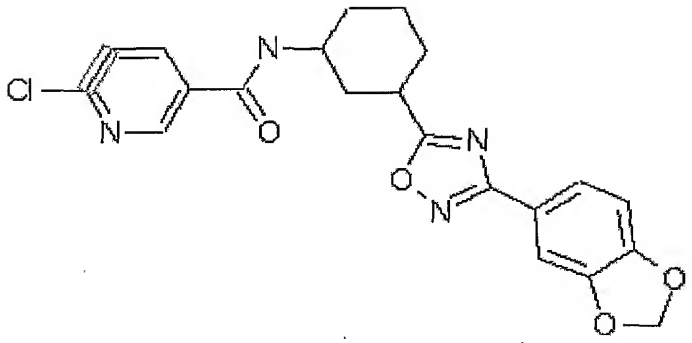


FIG. 136

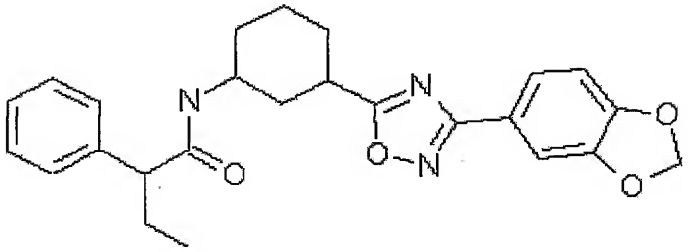


FIG. 137

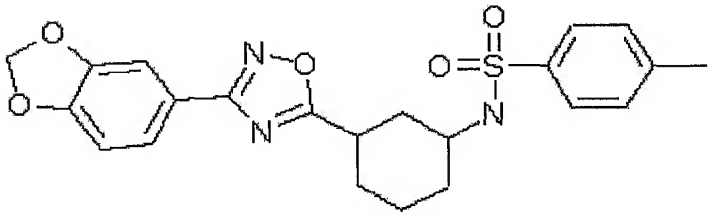


FIG. 138

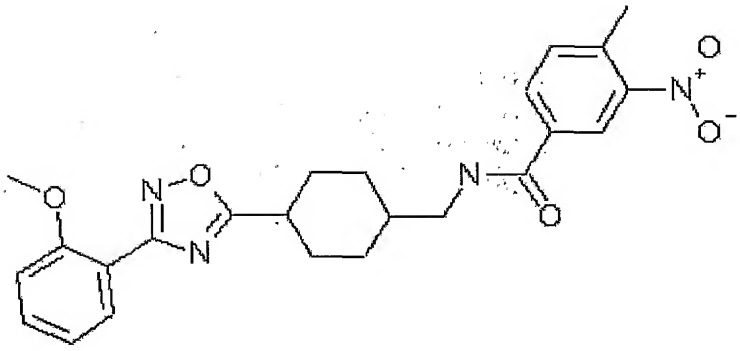


FIG. 139

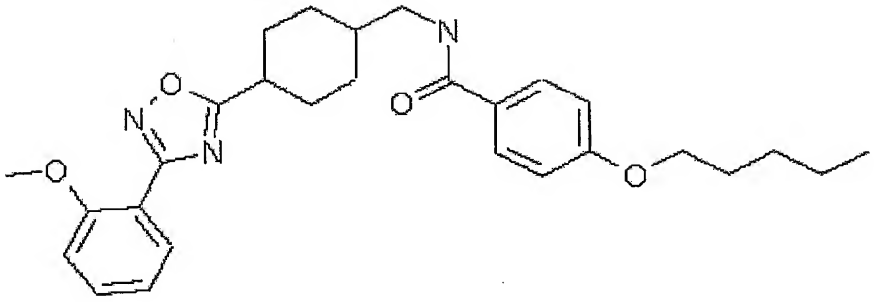


FIG. 140

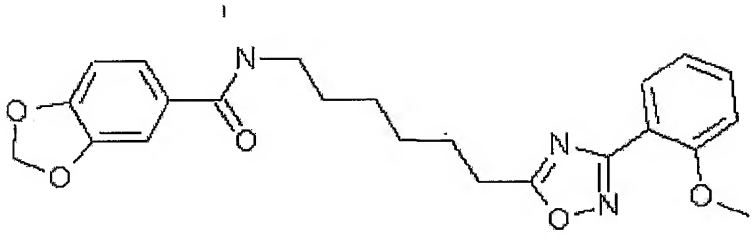


FIG. 141

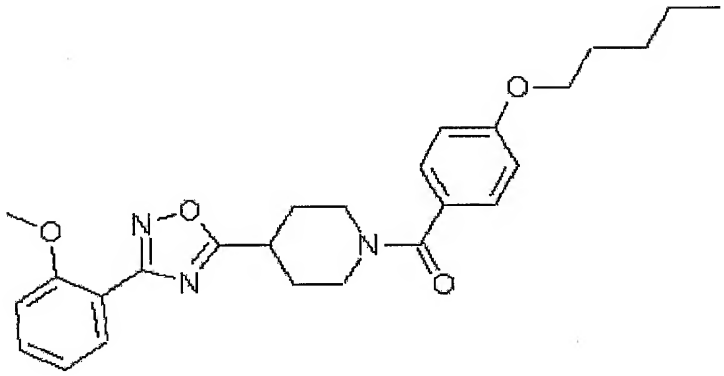


FIG. 142

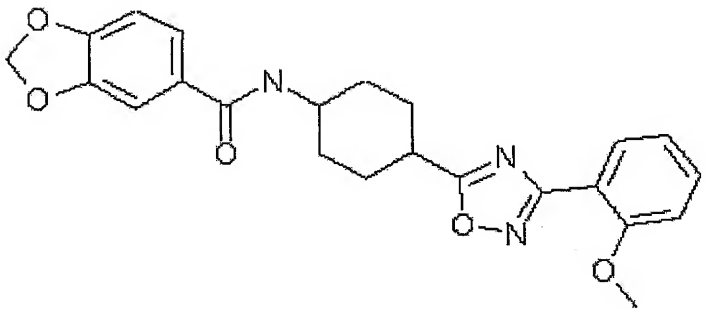


FIG. 143

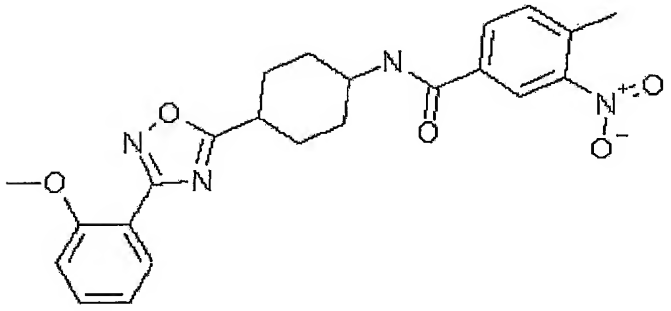


FIG. 144

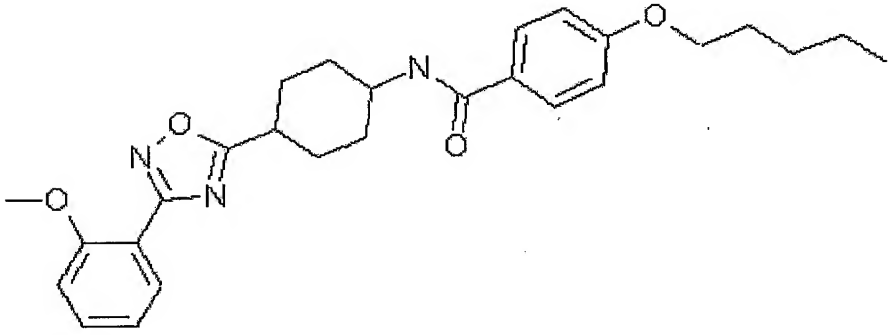


FIG. 145

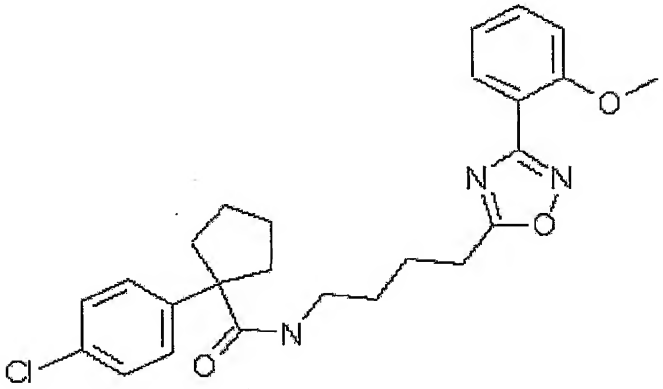


FIG. 146

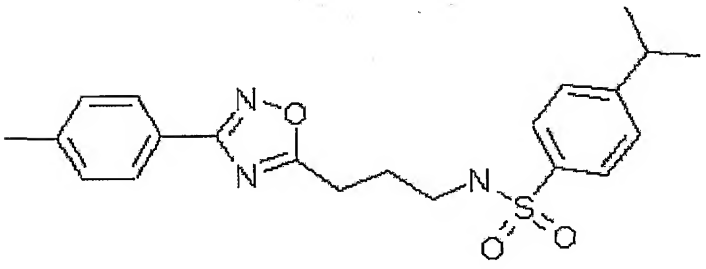


FIG. 147

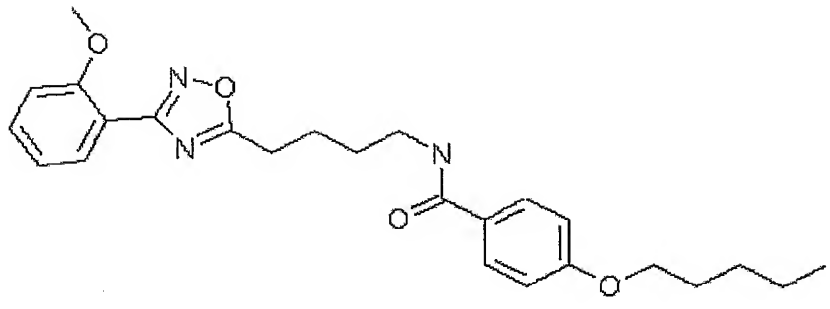


FIG. 148

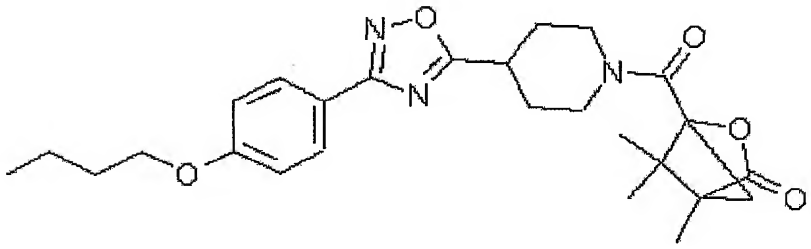


FIG. 149

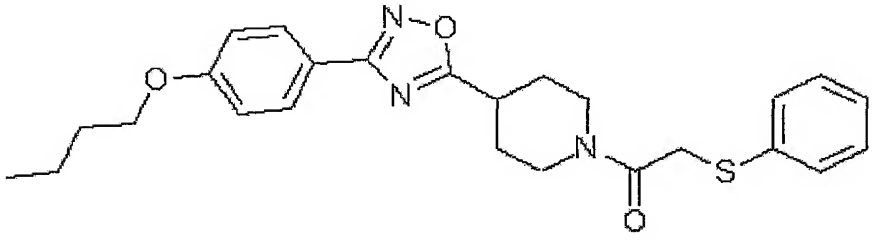


FIG. 150

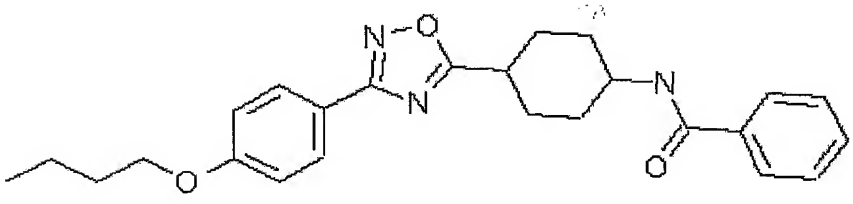


FIG. 151

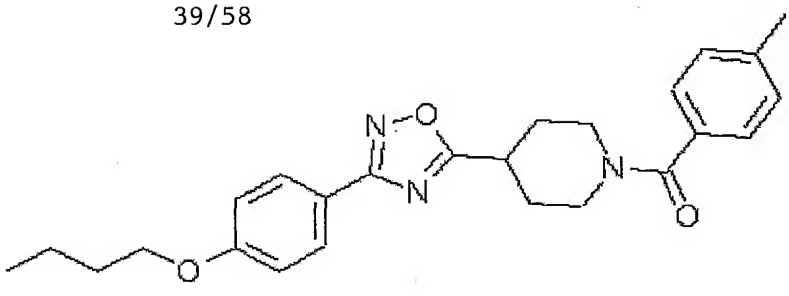


FIG. 152

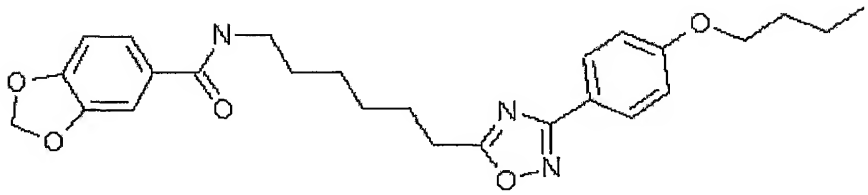


FIG. 153

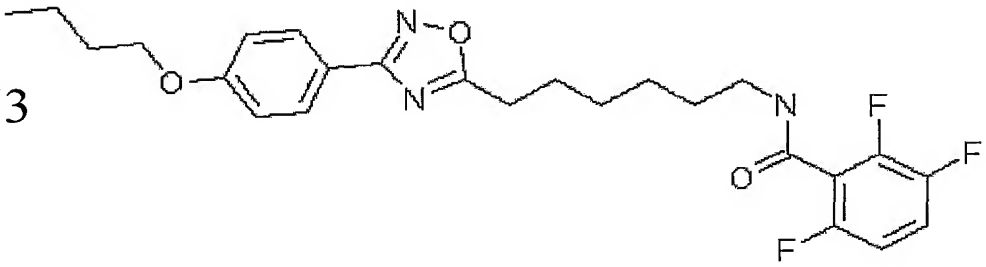


FIG. 154

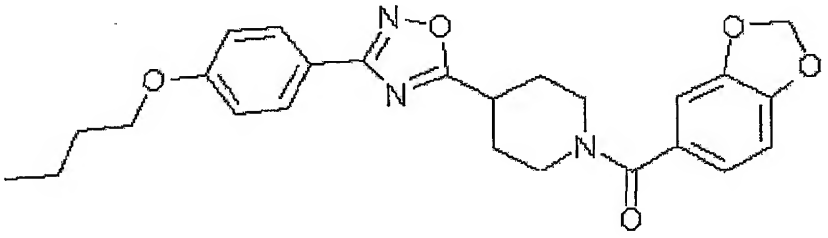


FIG. 155

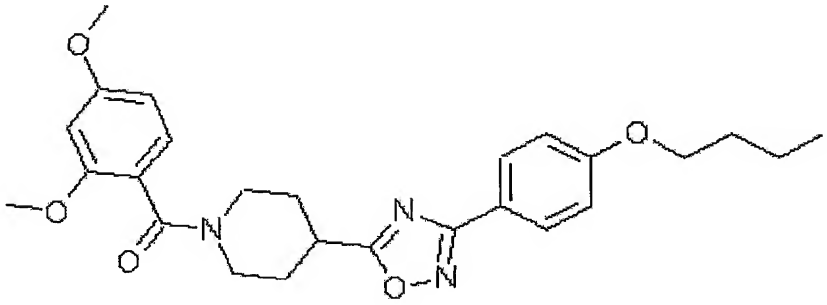


FIG. 156

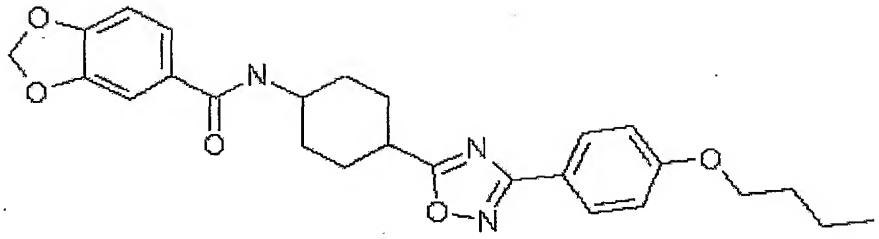


FIG. 157

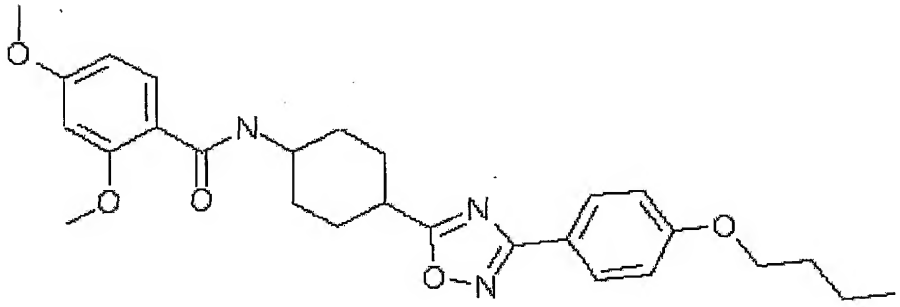


FIG. 158

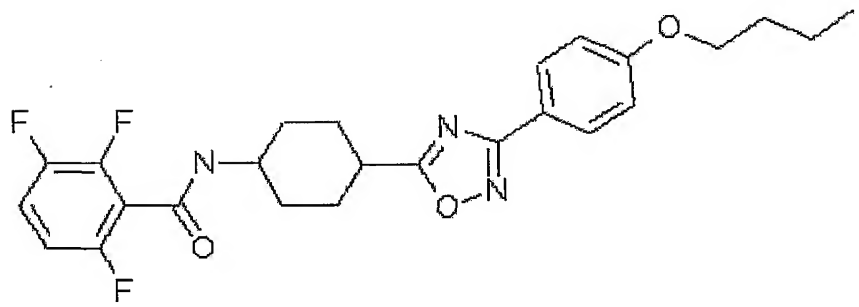


FIG. 159

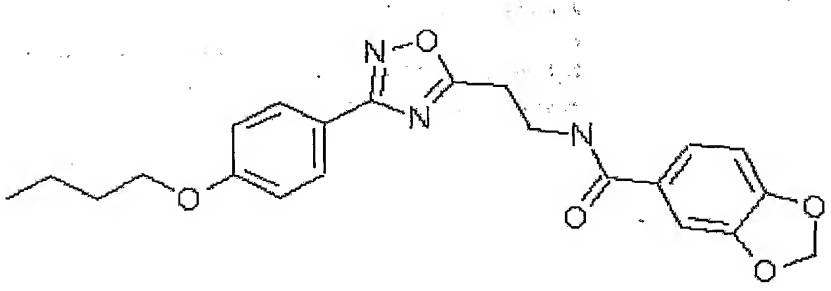


FIG. 160

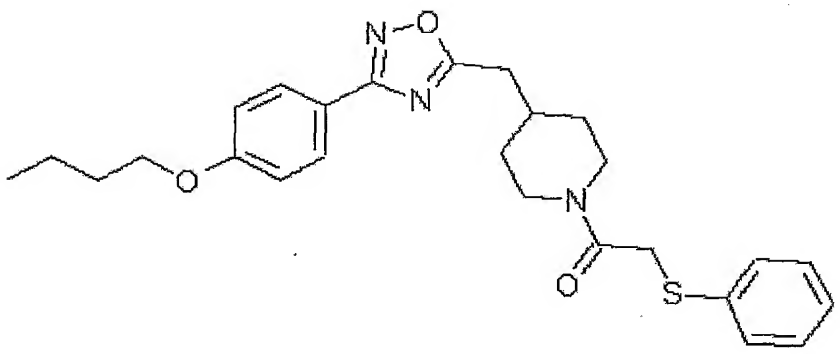


FIG. 161

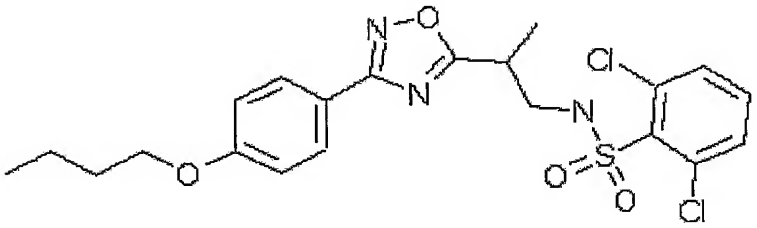


FIG. 162

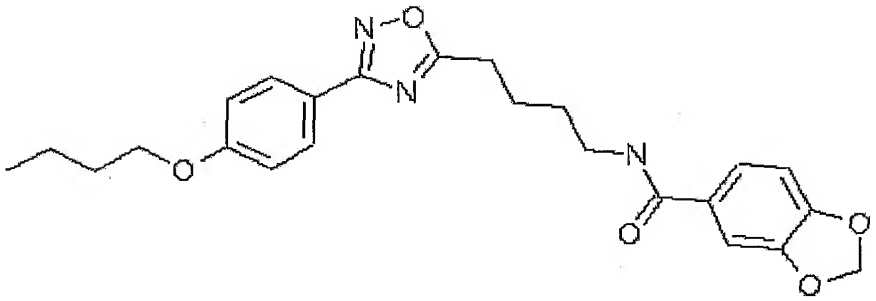


FIG. 163

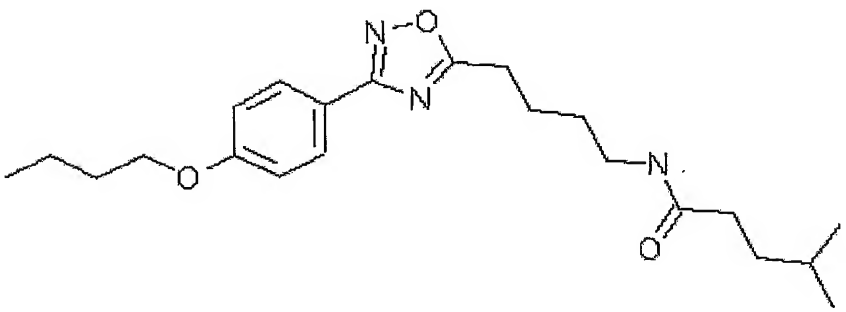


FIG. 164

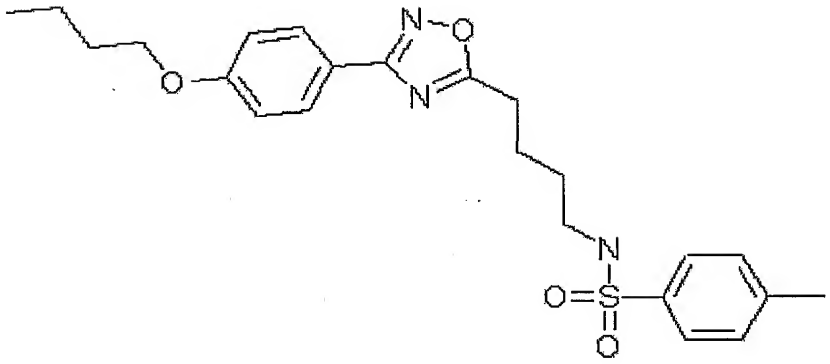


FIG. 165

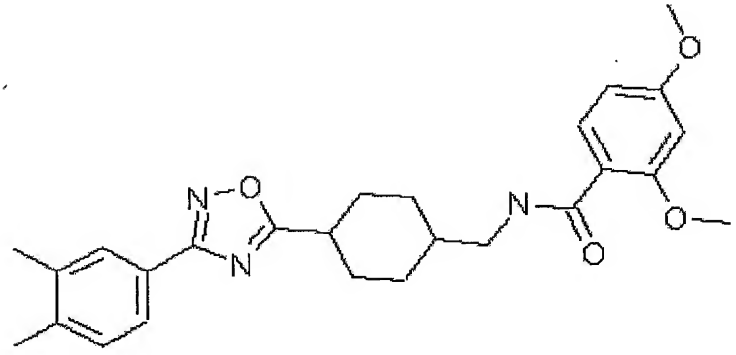


FIG. 166

FIG. 167

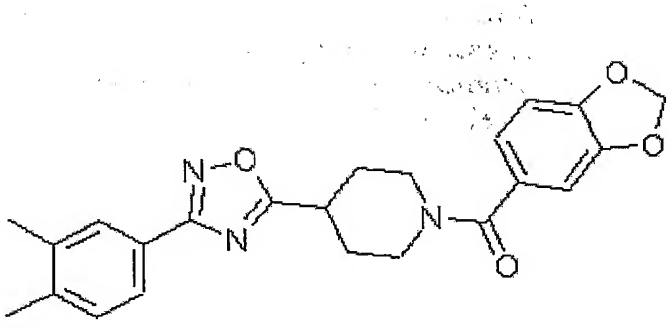


FIG. 168

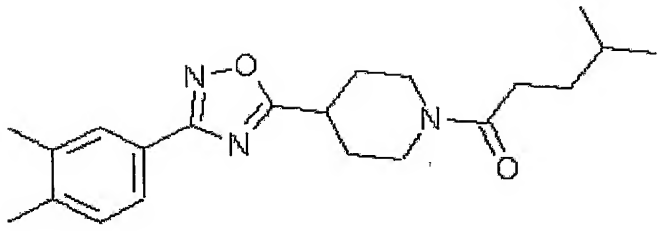


FIG. 169

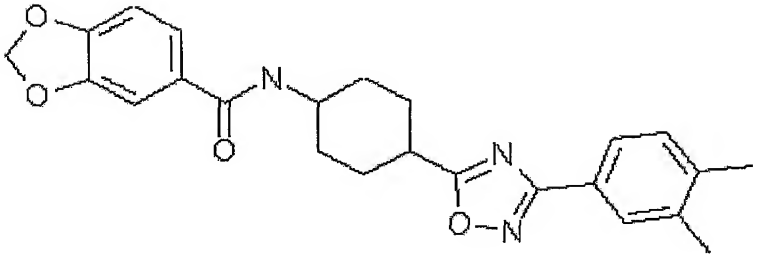


FIG. 170

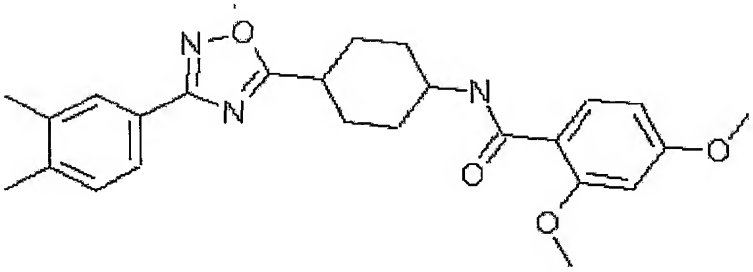


FIG. 171

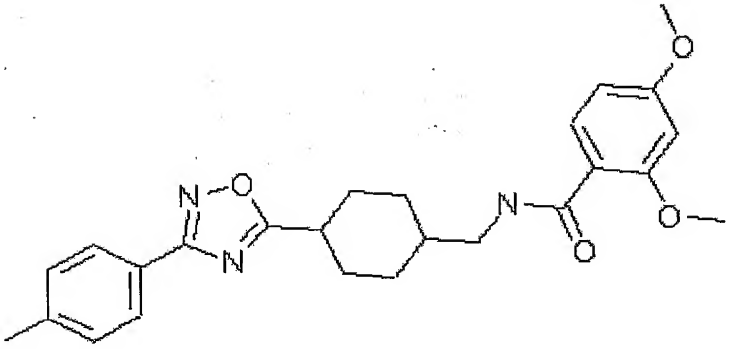


FIG. 172

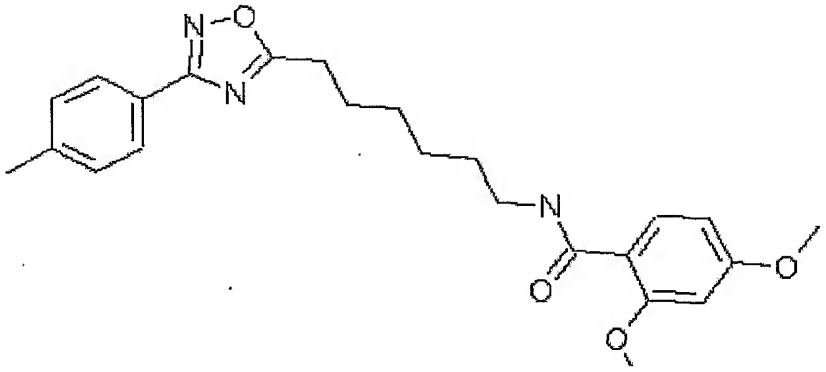


FIG. 173

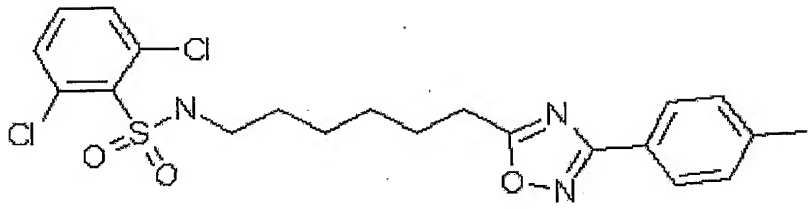


FIG. 174

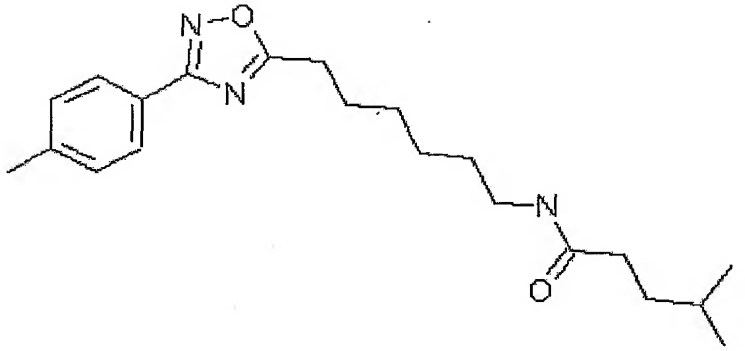


FIG. 175

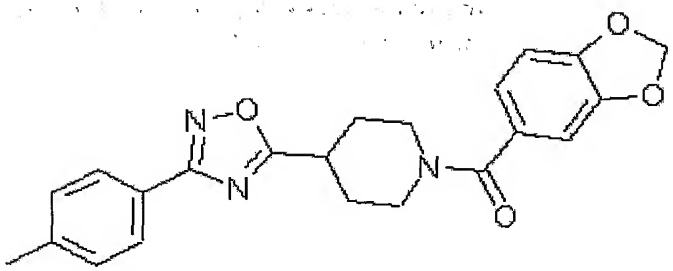


FIG. 176

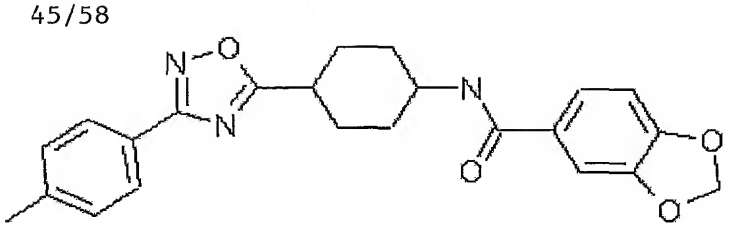


FIG. 177

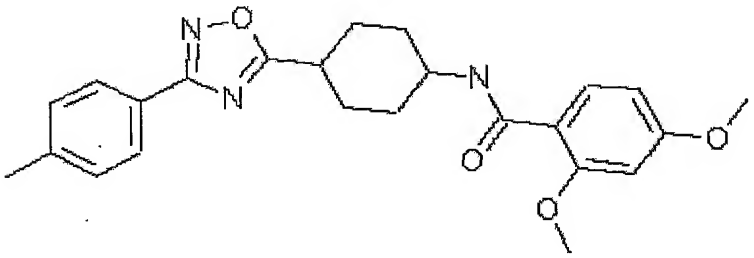


FIG. 178

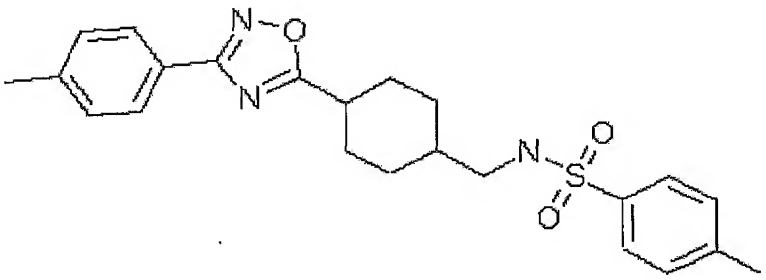


FIG. 179

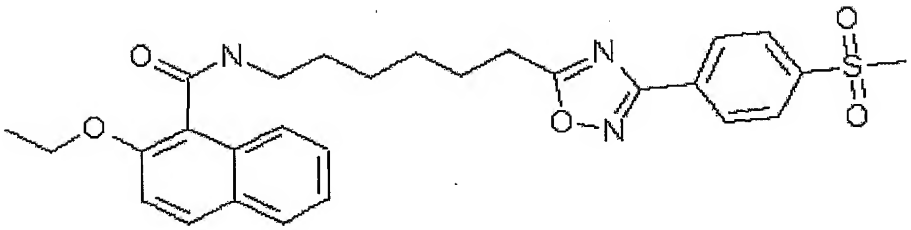


FIG. 180

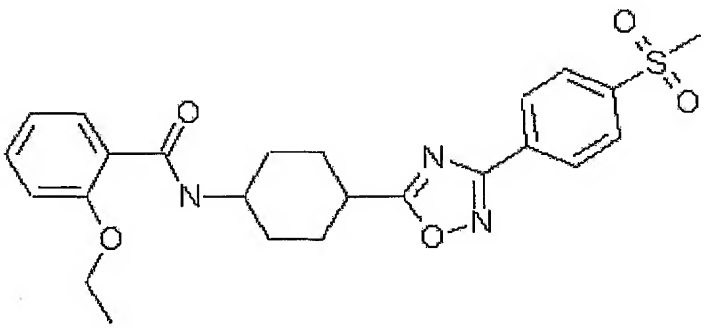


FIG. 181

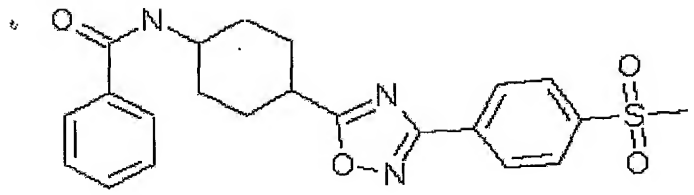


FIG. 182

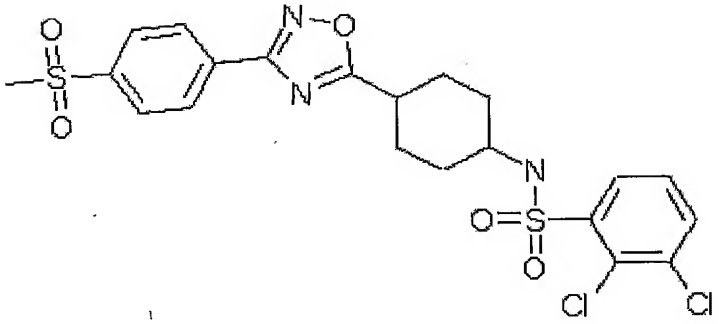


FIG. 183

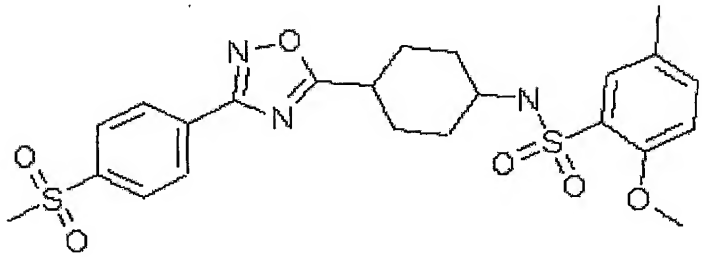


FIG. 184

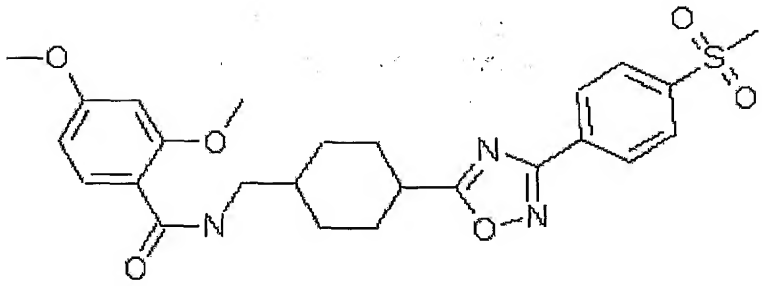


FIG. 185

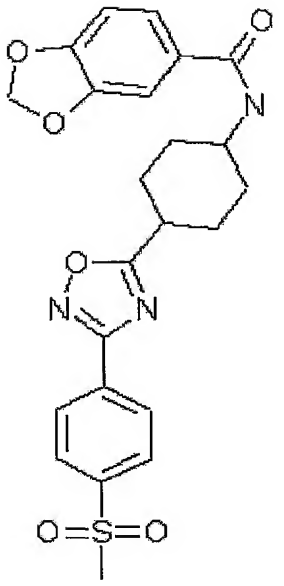


FIG. 186

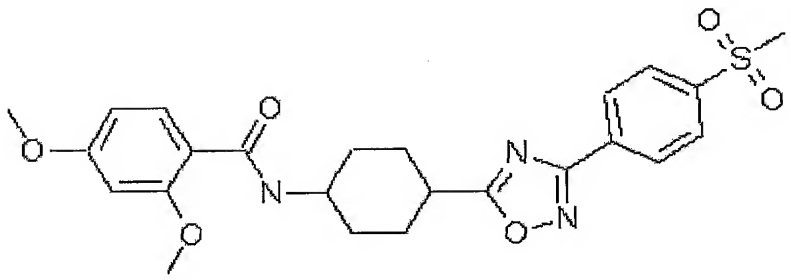


FIG. 187

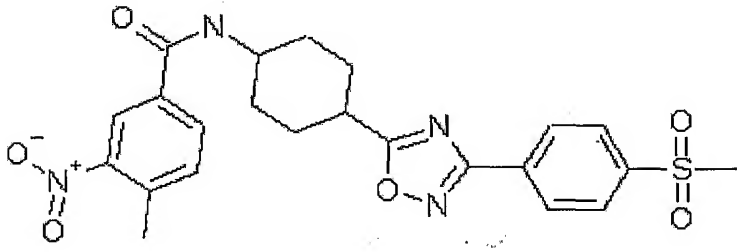


FIG. 188

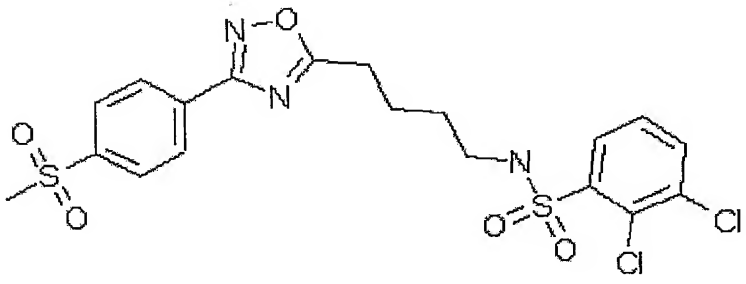


FIG. 189

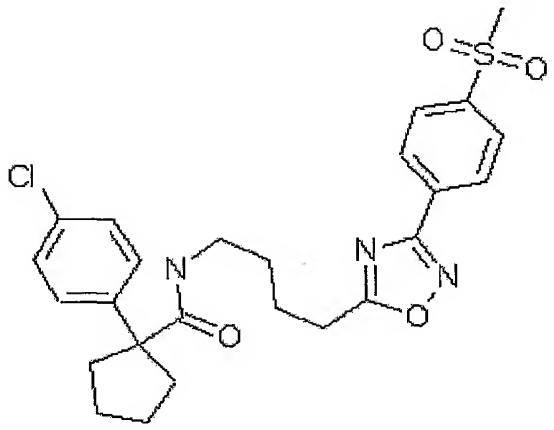


FIG. 190

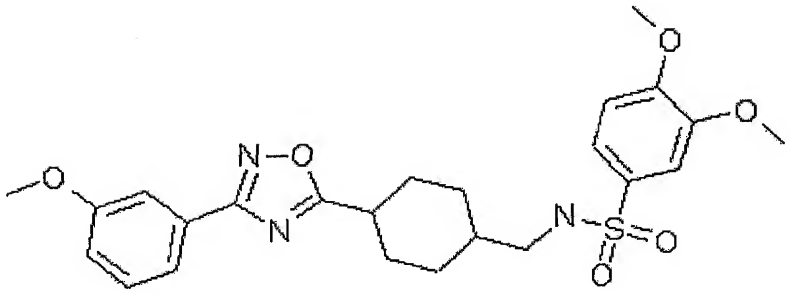


FIG. 191

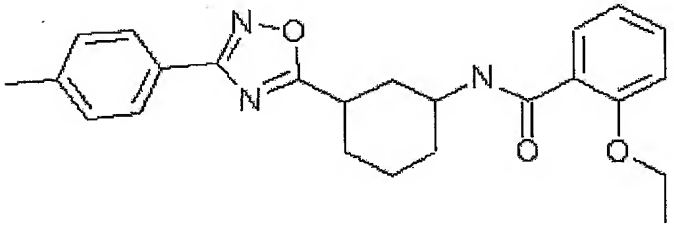


FIG. 192

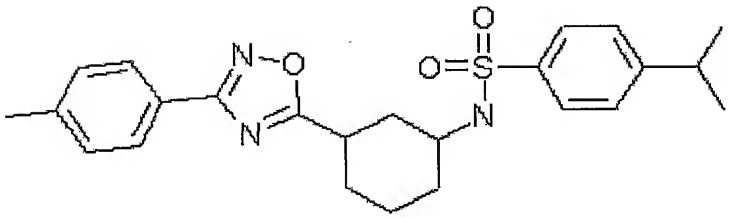


FIG. 193

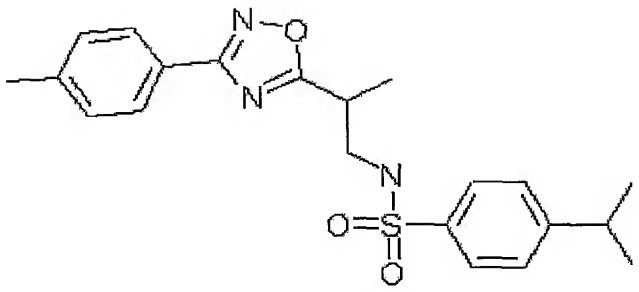


FIG. 194

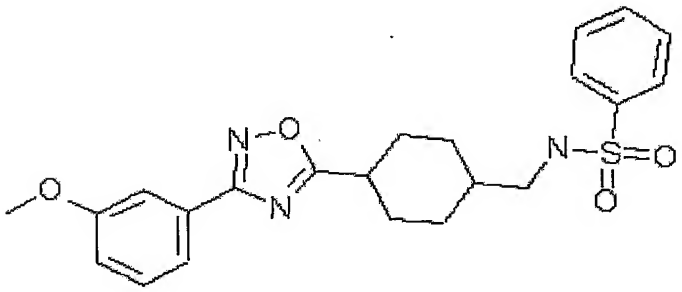


FIG. 195

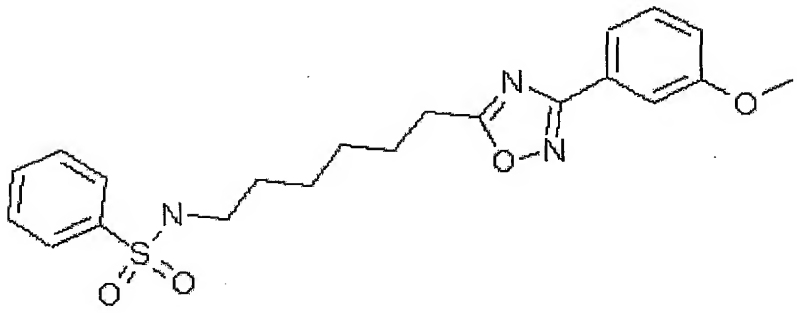


FIG. 196

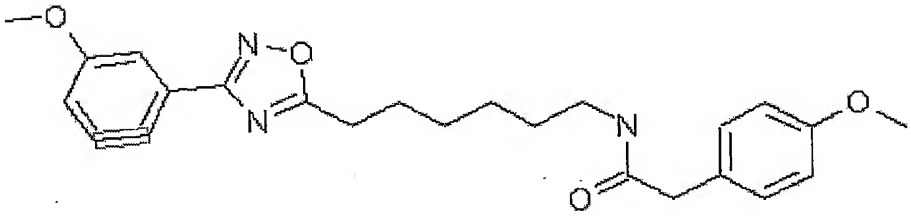


FIG. 197

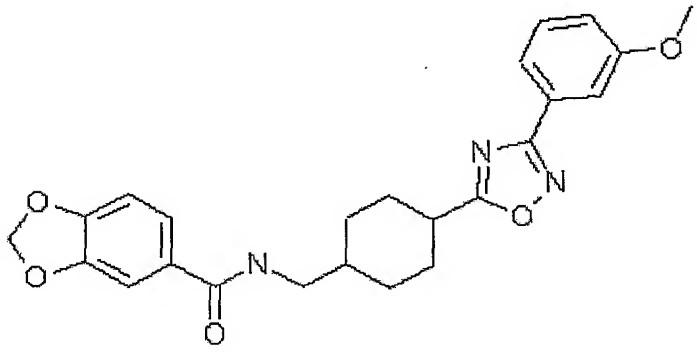


FIG. 198

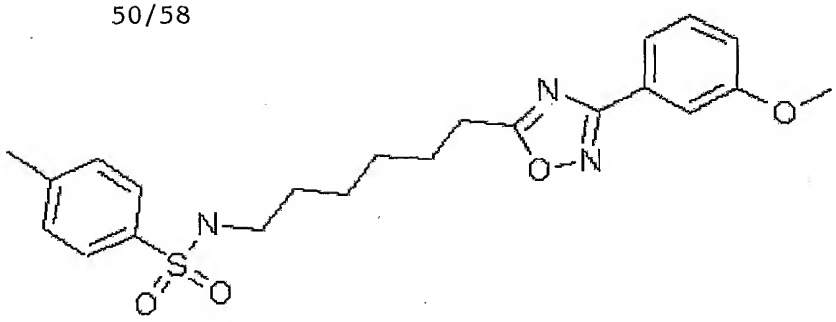


FIG. 199

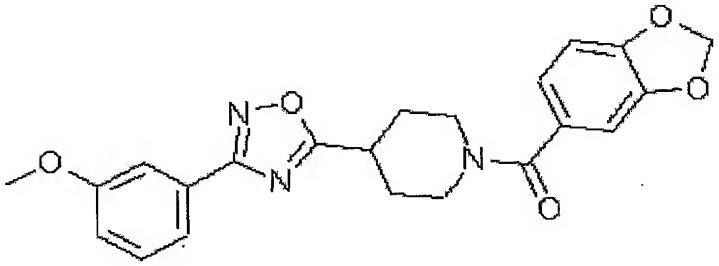


FIG. 200

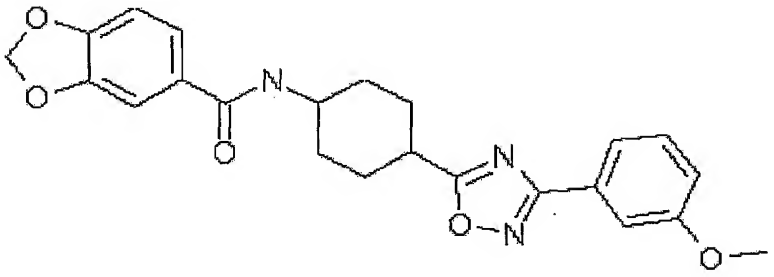


FIG. 201

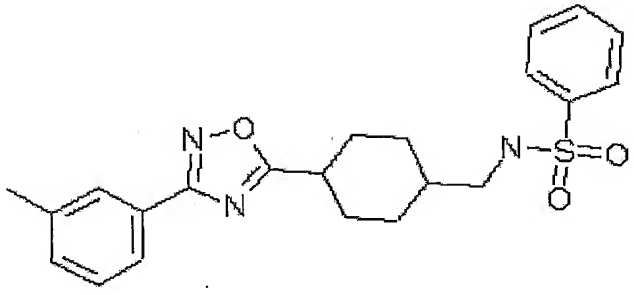


FIG. 202

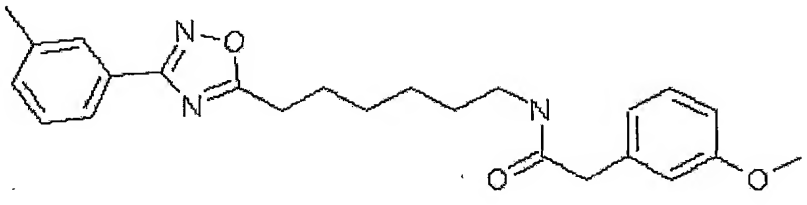


FIG. 203

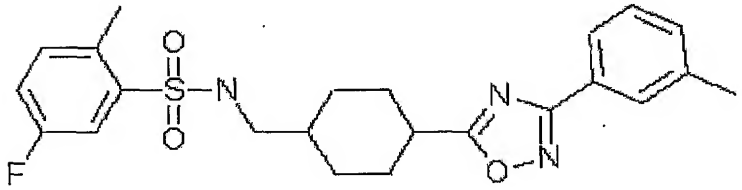


FIG. 204

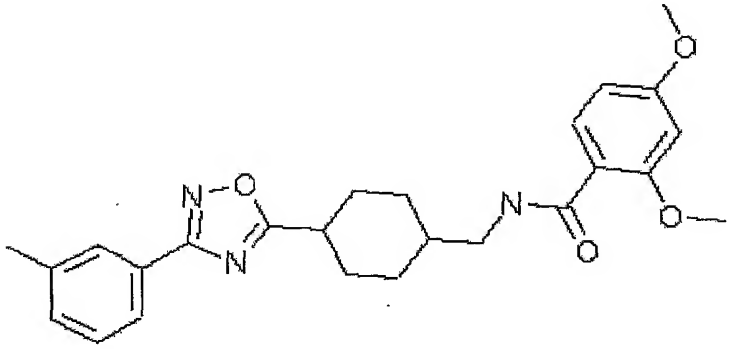


FIG. 205

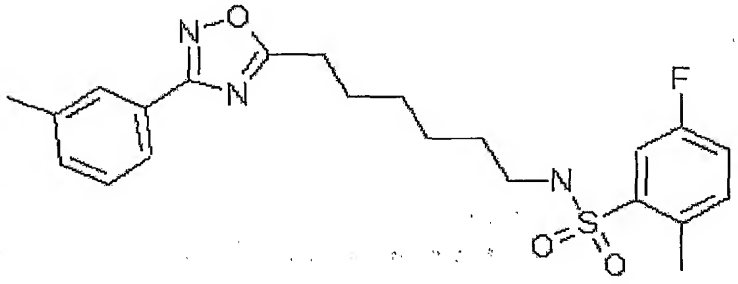


FIG. 206

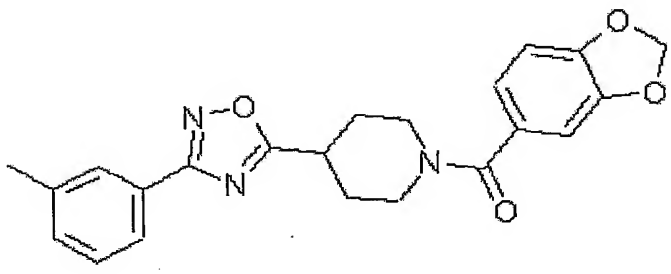


FIG. 207

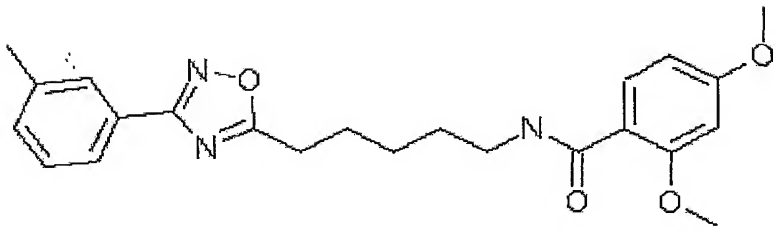


FIG. 208

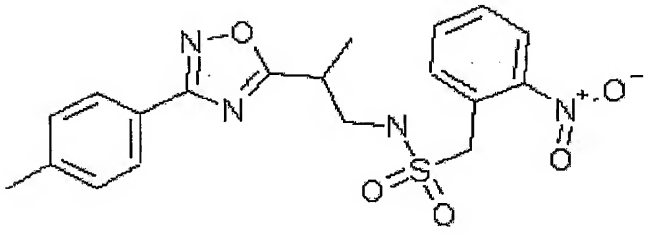


FIG. 209

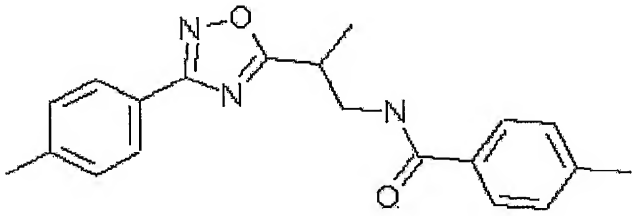


FIG. 210

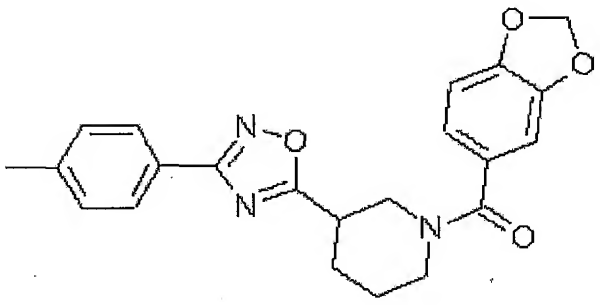


FIG. 211

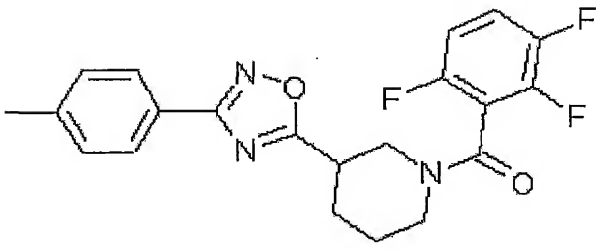


FIG. 212

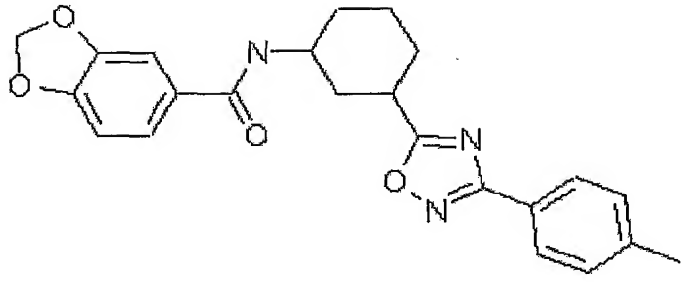


FIG. 213

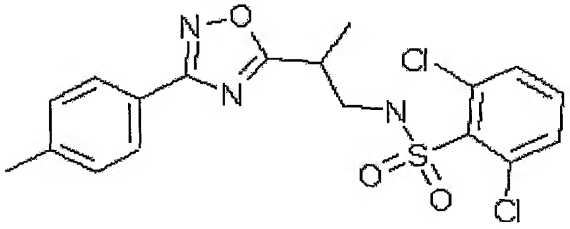


FIG. 214

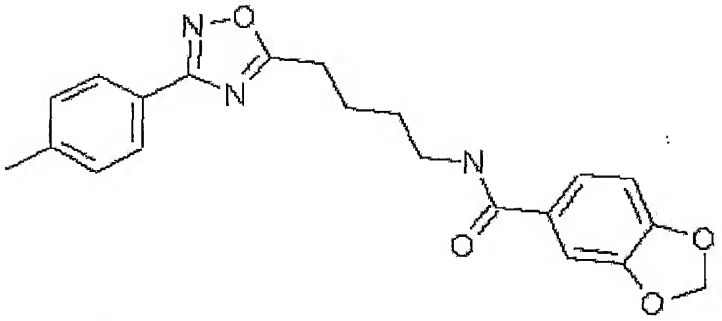


FIG. 215

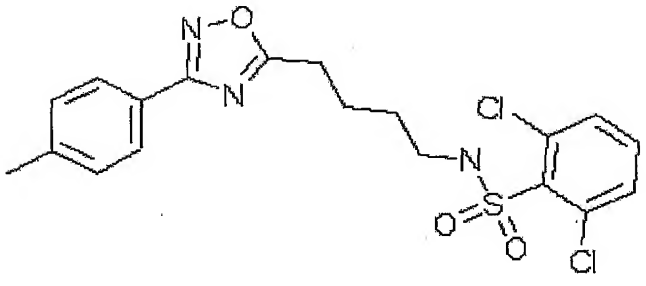


FIG. 216

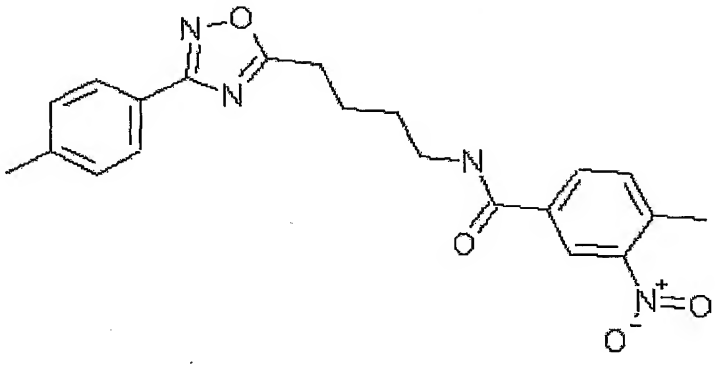


FIG. 217

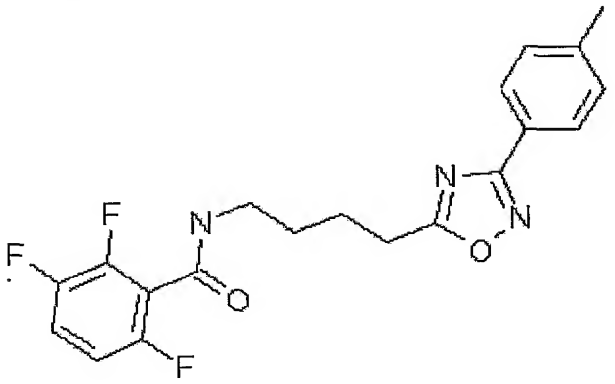


FIG. 218

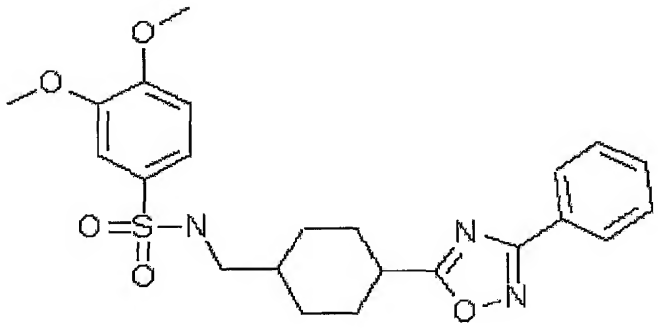


FIG. 219

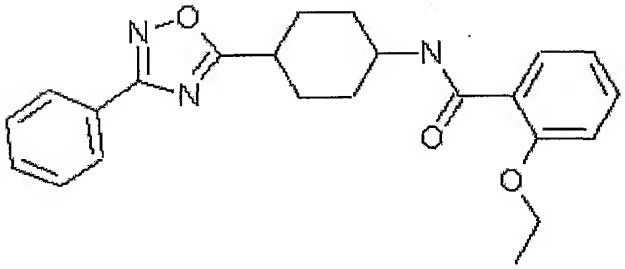


FIG. 220

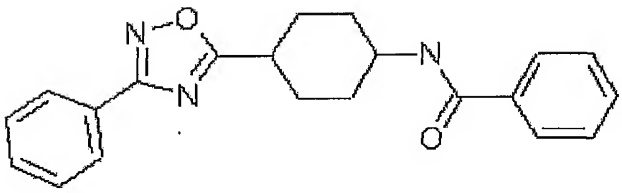


FIG. 221

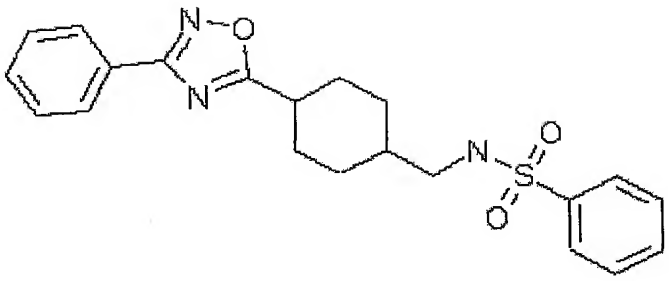


FIG. 222

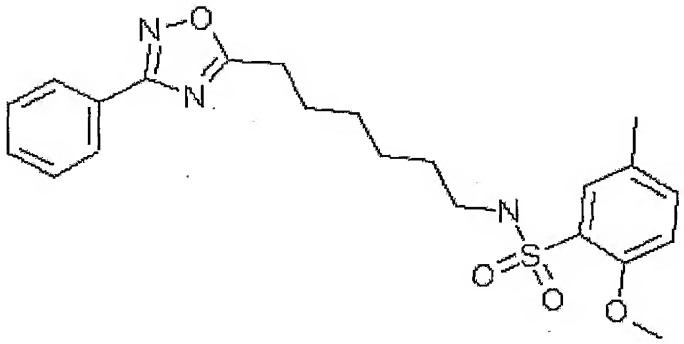


FIG. 223

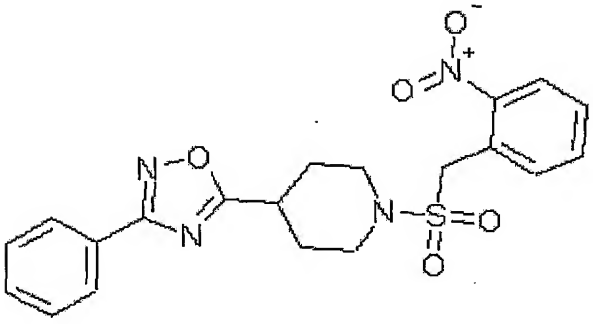


FIG. 224

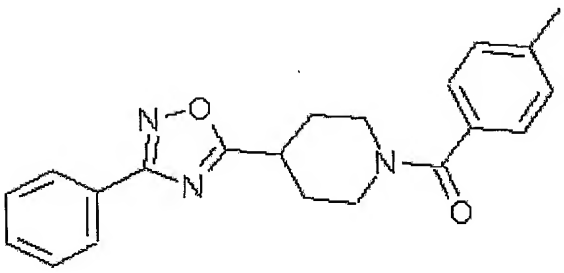


FIG. 225

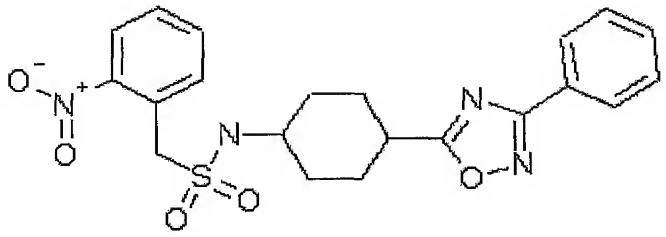
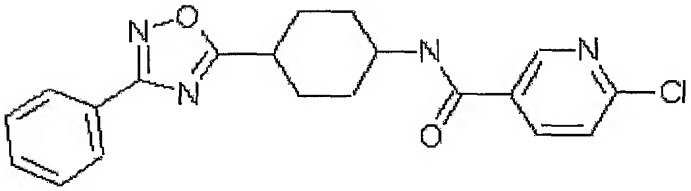


FIG. 226



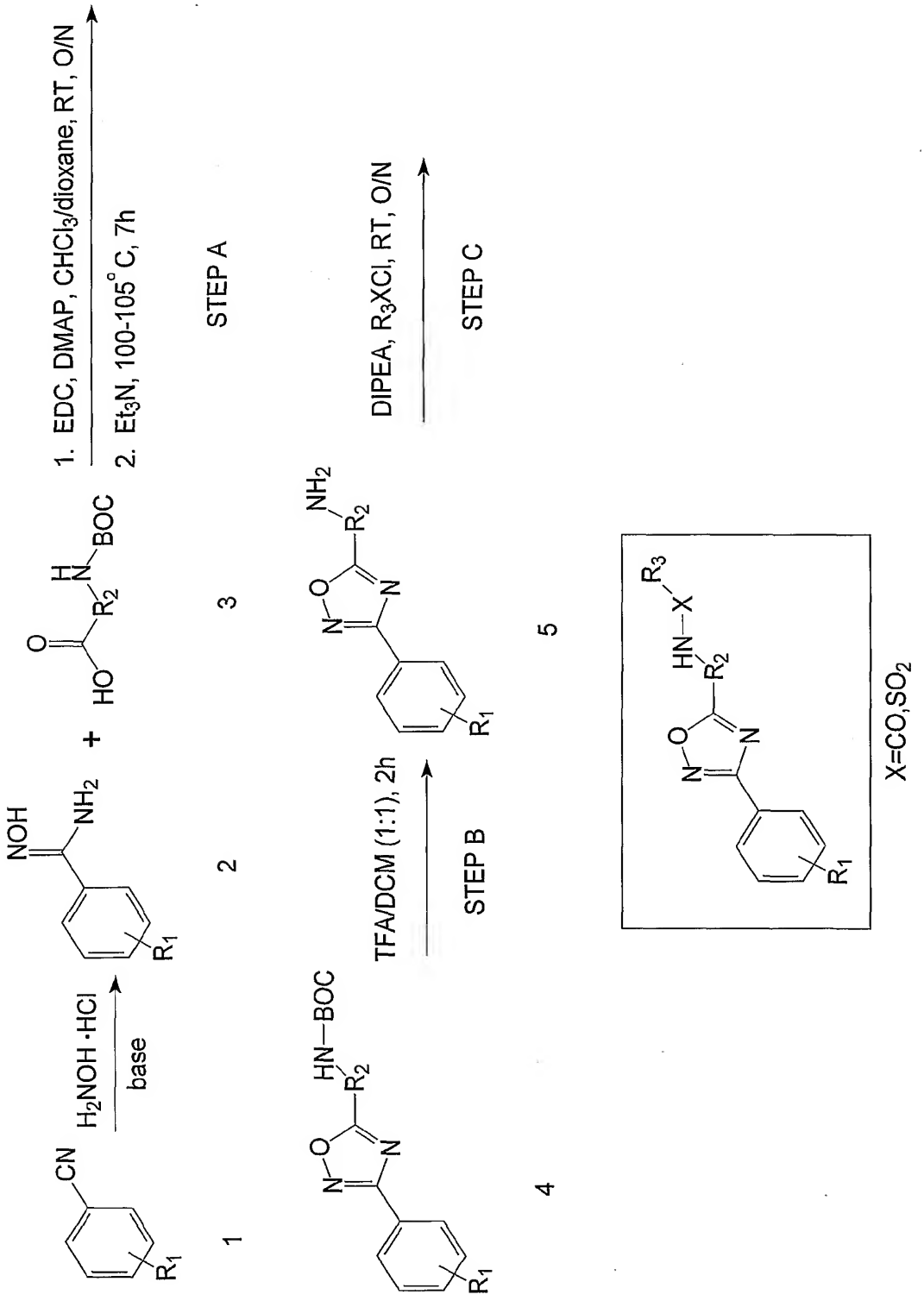

1. EDC, DMAP, CHCl3/dioxane, RT, O/N
2. Et3N, 100-105° C, 7h
STEP A
H2NOH ·HCl
base
TFA/DCM (1:1), 2h
STEP B
DIPEA, R3XCl, RT, O/N
STEP C
X=CO,SO2
1
2
3
4
5
6

FIG. 227

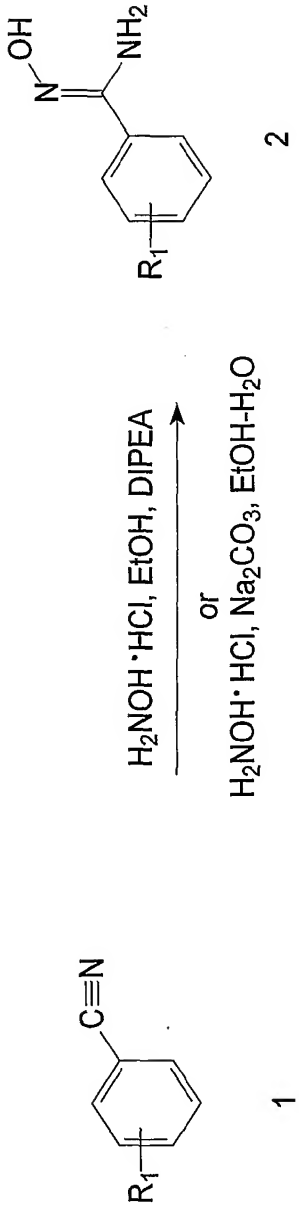


FIG. 228

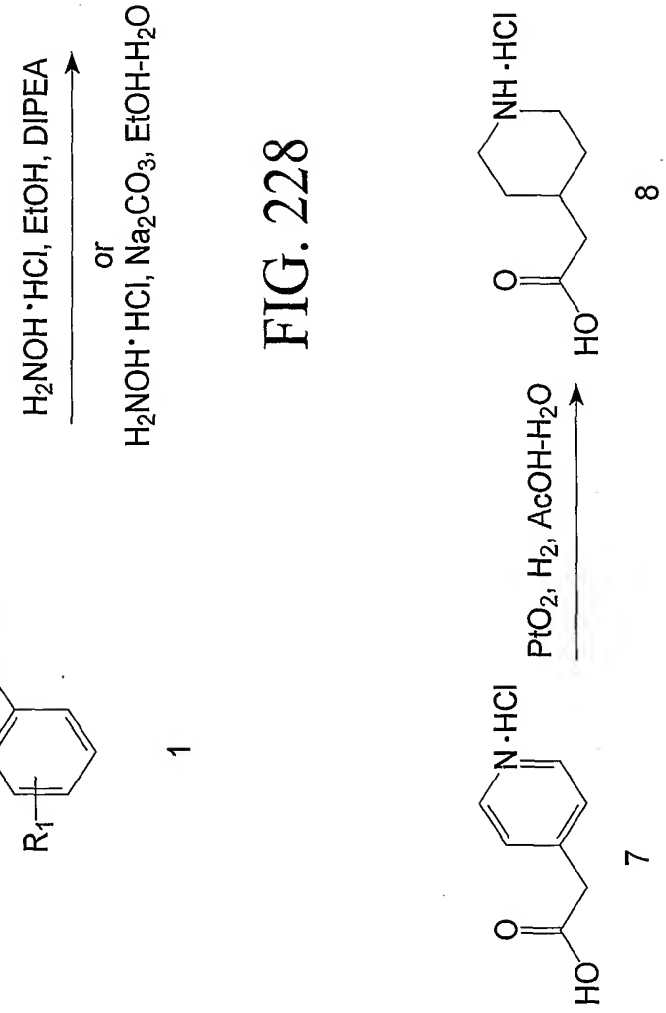


FIG. 229

INTERNATIONAL SEARCH REPORT

Inter I Application No
PCT/US 01/02848

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A01N43/836

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, EPO-Internal, PAJ, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 985 904 A (ERDELEN CHRISTOPH ET AL) 16 November 1999 (1999-11-16) column 26, line 64 -column 26, line 65; claims	1

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
3 April 2001	10/04/2001

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Fax: (+31–70) 340–3016

Authorized officer
Donovan-Beermann, T

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inter[illegible] Application No
PCT/US 01/02848

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5985904 A	16-11-1999	DE 4401108 A	20-07-1995
		AU 696288 B	03-09-1998
		AU 1455095 A	01-08-1995
		BR 9506515 A	09-09-1997
		CA 2181184 A	20-07-1995
		CN 1138858 A,B	25-12-1996
		WO 9519353 A	20-07-1995
		EP 0740663 A	06-11-1996
		FI 962857 A	15-07-1996
		HU 74714 A	28-02-1997
		JP 9507496 T	29-07-1997
		NO 962952 A	12-07-1996
		NZ 278591 A	26-02-1998
		TR 28098 A	08-01-1996
		ZA 9500305 A	21-09-1995